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RETROPERITONEAL SARCOMA.

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In a paper that appeared in this Journal[1] for March, 1900, the writer published a series of conclusions based upon the study of 61 cases of sarcoma originating in the retroperitoneal space. Since then I have had the opportunity of observing 3 new cases of retroperitoneal sarcoma, and have collected a supplementary series of 32 cases, making a grand total of 96 cases.

The reports of my own cases are as follows:

Case I.—*Female, white, aged eighty years; abdominal tumor in the upper central region that was thought to be an enlargement of the liver due to passive congestion; no cachexia; course fifteen months; death from acute bronchitis. Autopsy. Pathological diagnosis: spindle-cell sarcoma of the retroperitoneal space growing from the connective tissue around the cœliac axis. The colon lay upon the anterior surface of the tumor, and the stomach was displaced forward to the left.*

The patient was a woman, aged eighty years, who had been bedridden for some twenty years on account of an intracapsular fracture of the femur. She was a private patient of Dr. Musser, with whom I had the privilege of attending her. There were the usual arterial changes due to age. Her heart was considerably enlarged, both to the right and left, and there was evidently some degeneration of the myocardium.

[1] "A Critical Summary of the Literature of Retroperitoneal Sarcoma," The American Journal of the Medical Sciences, March, 1900.

About eighteen months before her death we noted that apparently her liver was enlarged. The interval of rapid enlargement was about three months, and at the end of this time the mass in her abdomen, that we took to be the liver, was as large as it was at any time during the fifteen months that intervened before her death. The abdominal mass very closely resembled the liver, and we considered it to be an hepatic enlargement due to passive congestion. The mass did not move freely on respiration, but we explained this by the fact that her respirations were very shallow, and were probably not sufficiently strong to move the enlarged liver up and down.

For over a year we examined the mass at very frequent intervals and never noticed anything that caused us to doubt our diagnosis.

The patient was not cachectic, and the presence of the abdominal tumor did not seem to have any effect upon her general health. It caused her some slight discomfort and pain, but that was all. If the idea of malignant growth had occurred to us we would probably have excluded it on account of the absence of wasting and cachexia.

A note made six months before her death upon the size and position of the liver is as follows:

"The liver is much enlarged and extends to the level of the umbilicus in the midclavicular line. The right lobe extends almost to the crest of the ilium, and there is very little if any movement of the lower edge in respiration. The breathing is very shallow, and there is hardly any movement of the diaphragm. The upper dulness of the liver commences at the seventh rib. The surface is hard and a little rough on the right side. The left lobe apparently extends to a point just below the umbilicus."

The patient had a goitre of moderate dimensions. She died eighteen months after the abdominal growth was first noticed, of an acute capillary bronchitis.

An autopsy was performed twelve hours after death. There was much arterial sclerosis involving the coronary arteries and considerable degenerative change in the myocardium.

The notes upon the abdomen were as follows.

There was a tumor as large as a child's head, eight inches in diameter, originating behind the peritoneum in the upper central portion of the abdomen. It grew just back of the lesser curvature of the stomach. The left lobe of the liver lay flattened out along the upper border of the mass. The pressure that this part of the liver had undergone had caused some atrophy, and the edge of the organ was considerably thinned. The right lobe of the liver was thickened and elongated and extended to the crest of the ilium. Its surface was rough and typically hobnailed.

Microscopic examination of the growth showed that it was a compact spindle-cell sarcoma. The tumor had a well-marked capsule, which sent trabeculæ of fibrous tissue in various directions to the growth. The bloodvessel supply was not profuse. There was

considerable hemorrhage in various areas of the tumor, and in many places there were the usual blood channels without walls characteristic of sarcoma.

The liver showed an extreme degree of interlobar cirrhosis with atrophy of the liver cells, and proliferation of the bile-ducts. In the lappet of the liver, which was flattened against the tumor, the liver substance was almost entirely destroyed, and the anterior edge of the organ had been converted into fibrous tissue rich in round cells, with here and there a bloodvessel and proliferated bile-ducts.

The stomach lay against the lower and anterior edge of the tumor and was carried forward, downward, and to the left by the growth of the tumor behind it. The small intestines were pushed downward. The hepatic flexure of the colon was displaced downward, while the splenic flexure remained in approximately its normal condition, so that the transverse colon ran diagonally upward across the abdomen and lay against the lower anterior surface of the tumor somewhat overlapping the stomach. The tumor appeared to spring from near the sheath of the great vessels above the cœliac axis and adherent to them. It lay just above the pancreas, but did not involve it.

The kidneys and adrenals had no connection with the tumor. The retroperitoneal lymph glands above and below the tumor were not affected. The tumor was freely movable, and might easily have been moved on respiration if the breathing had been strong enough. It was covered by peritoneum, which was somewhat thick and shining. It was nearly round and was encapsulated. On section it was white and hard, except for a small area in the centre which had softened. In several places it was distinctly lobulated. The lower border extended to within one inch of the umbilicus. The tumor's close connection with and its adherence to the left lobe of the liver, together with the enlargement of the right lobe of that organ, gave the whole mass of the tumor and the liver taken together a shape that approximated the general shape of an enlarged liver.

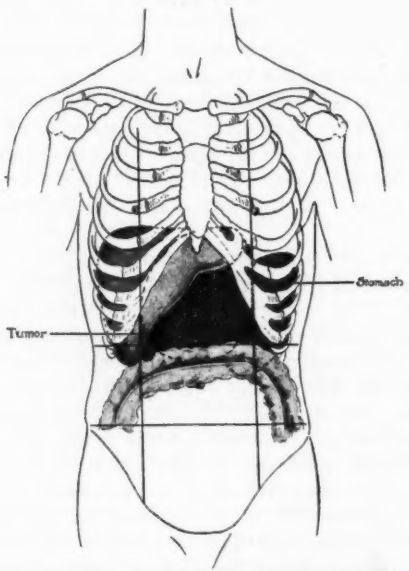
The lack of respiratory movement was explained by the weakness of breathing and absence of the movement of the diaphragm.

The case illustrates well several points in the diagnosis of retroperitoneal sarcoma. The position of the colon and stomach was very characteristic. The transverse colon lay upon the anterior and lower surface of the growth, and was pushed forward and downward. The stomach was pushed outward and slightly upward. The onset was very insidious and without objective symptoms. The tumor was elastic and resembled the liver very closely in its physical characteristics, so that the physical examination entirely misled us. It is probable that if the patient had been stronger and had taken a more liberal diet, she would have experienced some disturbance of digestion on account of the interference with the functions of the stomach and colon.

It is probable also that if the patient had been able to take a long breath the movement of the diaphragm would have imparted some motion to the tumor, since the growth was not as firmly fixed as retroperitoneal growths usually are. Indeed, the tumor was quite easily movable at the autopsy.

The tumor differed from other retroperitoneal sarcomata in its protracted course, in the absence of areas of softening and degeneration, which could be detected by physical examination, and in the small effect that it had upon nutrition. The advanced age of

FIG. 1.



CASE I.—Retroperitoneal sarcoma. The transverse colon is pushed forward and crosses the anterior and lower half of the tumor. The stomach is pushed forward and to the left. Compare Fig. 4.

the patient may explain two of these points of difference, since the tissue changes of advanced age are necessarily slower than in youth, and if cell metabolism had been more active there would probably have been wasting and cachexia enough to have caused the death of the patient from exhaustion in a much shorter time than fifteen months.

As far as we could determine the presence of the tumor had very little effect upon the length of life.

CASE II.—*A white girl, aged four years. Six months after a fall which caused a hard blow upon the upper portion of the abdomen,*

there was enlargement of the left side of the abdomen accompanied by loss of weight and cachexia. Tumor and left kidney removed by operation; death in several months; metastasis to skin of the thorax. Pathological diagnosis: Spindle-cell sarcoma, which sprang from the capsule of the left kidney. Tumor was centrally degenerated.

Case II. has already been reported before the Pathological Society of Philadelphia as an "Endothelioma of the Retroperitoneal Space." Further study of the case convinces me that I was mistaken in my first diagnosis, and that the growth was a round-cell and spindle-cell sarcoma.

The patient was four years old. She had always been quite well and active. One year before admission she fell from a considerable height across a rail fence, striking the rail with her abdomen. Six months after this enlargement of the left side of the abdomen was noticed. This increased steadily and caused a marked protrusion. Her general health began to fail, and she rapidly lost weight. Examination on admission to the hospital showed a large, firm, and smooth mass occupying the entire left side of the abdomen and extending about one inch to the right of the median line. The day after admission Dr. Willard operated and removed the tumor, which occupied the whole left half of the abdomen and lay behind the peritoneum. The left kidney was adherent to the mass and was removed with it. The child was much shocked, but recovered from the effect of the operation.

The patient went home and for a time was perfectly well. The growth, however, soon recurred. The physician in attendance reported metastasis in the skin of the thorax near the heart, but from the rapid loss of strength of the patient it is probable that there was some visceral involvement as well. She died three months after the operation. There was no autopsy.

The tumor removed at operation was a large oval mass measuring 15 cm. at its largest diameter, 7 cm. in its transverse diameter, and 22 cm. in its greatest circumference. The surface was smooth and firm. The tumor appeared to be made up of a number of spherical masses, averaging 3.5 cm. in diameter. These spheres around the edge of the mass were firm and hard, and on section they were pinkish-white in color. There was a well-defined framework of connective tissue surrounding these bodies and separating them from each other. The centre of the mass was much degenerated, and the central cavity was filled with a cheesy semifluid material. There did not appear to have been any extensive hemorrhage, although the undegenerated portions were studded here and there with small hemorrhagic spots.

The tumor was closely adherent to the left kidney and lay anterior to it and below it. The kidney was compressed and flattened from front to back. On section it was pale and somewhat light in color. Sections of the cortex of the kidney immediately adjacent to the

tumor showed that the organ was considerably affected by the pressure of the growth. The capsule of the kidney was also much thickened and merged into the capsule of the tumor. In no place was there evidence that the neoplastic process had invaded the kidney or its capsule. The capsule of the tumor was about 2 mm. thick and sent trabeculæ between the tumor cells, so as to give the section a distinctly alveolar arrangement. The blood supply of the capsule was very abundant, while that of the tumor itself was fairly so.

Some of the bloodvessels in the tumor had the lack of true walls characteristic of sarcoma. Others had fairly perfect walls and carried with them a very delicate framework of fibrous tissue. The portion of the tumor nearest the kidney was traversed by bands of fibrous tissue and by collection of cells which had a distinctly columnar appearance. These cells were of varying shapes. Some forms had a deeply staining and large nucleus, while others had a distinctly oval nucleus. There was a very fine intracellular cement substance which was homogeneous and stained faintly with eosin.

The mass of the tumor was made up of round cells and spindle cells and was evidently a sarcoma of mixed type. There was considerable connective-tissue stroma dividing the growth into alveoli, but the fibrils of connective tissue did not run between the cells. The diagnosis of endothelioma was based upon the presence of columns of cells which were apparently endothelial in type and that ran through the tumor, suggesting lymph spaces. Further study, however, has convinced me that these columns were small bloodvessels with proliferation of their lining endothelium. Well-formed bloodvessels were very few in number and the greater part of the blood supply was furnished by blood channels with endothelial lining, but without true walls. The growth was evidently a sarcoma of mixed type, and apparently sprang from the capsule of the kidney or the fibrous tissue immediately adjacent to it. Apparently it had included a number of lymphatic glands.

The case is of interest, because the history of injury seems to bear a quite distinct relation to the beginning of the growth. The pathological anatomy agrees very closely with that found in most of the reported cases.

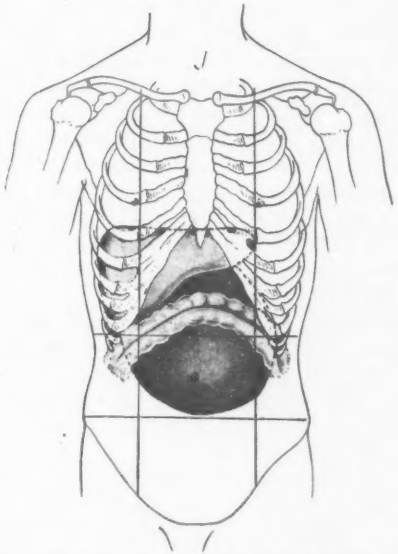
It is to be regretted that no record was kept of the physical examination or of the relation of the tumor to the mass. Its course was very rapid, though not more so than in a great many of these retroperitoneal sarcomata.

CASE III.—*White man, aged sixty-three years. Attacks of colic-like pains in the epigastrium commencing ten years before and becoming more frequent and severe until they resembled gastric crises. Six months before a tumor had appeared under the costal margin upon the right side. This grew rapidly until at the time of examination it was as large as a child's head. Œdema of the right ankle and leg;*

emaciation and cachexia. The tumor was immovable, hard, and nodular, with one spot of softening. The colon lay on the anterior upper surface of the tumor and separated it from the liver. Urine negative; no jaundice.

The third case was seen at the University Hospital through the courtesy of Dr. Musser. The diagnosis was not verified by operation or autopsy, but the history and the result of the physical examination presented a typical picture of what the study of the reported cases has taught one to expect. The case is reported with a tentative diagnosis.

FIG. 2.



CASE III.—Retroperitoneal sarcoma. The colon is pushed forward but crosses the upper half of the tumor instead of the lower half, as is usual in upper central retroperitoneal tumors.

The patient was a white man, aged sixty-three years, and a native of Virginia. He was healthy up to ten years ago, when he began to have attacks of colic-like pain in the upper abdomen. These attacks resembled those of gastralgia. He was not jaundiced, did not vomit, and there was no reason to suspect the presence of gallstones. The attacks occurred at long intervals until about a year before admission, when they became more frequent, and the pain radiated through the lumbar region. Six months before a tumor appeared just under the edge of the rib on the right side. About this time there was œdema of the right leg and ankle, which lasted about four

weeks. There was no pain in either leg. The patient had very frequent attacks of sharp pain over the tumor. There was no nausea or vomiting. He was much emaciated and cachectic, and suffered from constipation. The tumor was the size of a child's head and lay in the upper central portion of the abdomen. It extended slightly farther to the right than to the left. It was generally hard and nodular, although in the lower half there was a spot of softening with obscure fluctuation. The tumor was firmly fixed and immovable. The colon was full of gas and could be seen as well as mapped out by percussion. It ran over the upper anterior surface of the tumor, between it and the liver. The edge of the liver could be plainly felt just above the colon (Fig. 2). The patient refused operation and passed out of observation. Examination of the urine showed that the specific gravity was 10.16. It contained no albumin and no sugar, and it was negative microscopically.

The position of the colon showed quite clearly that the tumor was retroperitoneal. The fact that the colon lay between the tumor and the liver indicated that it had no connection with that organ. The absence of jaundice was against tumor of the head of the pancreas, and the hardness and solidity of the tumor excluded cyst of that organ or of any other structure. The growth was apparently a solid malignant retroperitoneal growth, and the diagnosis would seem to lie between a retroperitoneal tumor proper and a tumor originating in the adrenals or kidneys.

The result of urinary examination was against a growth of the kidney, but did not exclude it. The fact that the tumor was beginning to degenerate and soften was in favor of its being retroperitoneal sarcoma. The diagnosis must be a tentative one, but the picture that the case presented is very much in accord with that of a typical case of retroperitoneal sarcoma.

The notes of the following cases were given me by Dr. Howard J. Williams, of Macon, Georgia. I wish to express my very deep obligation to Dr. Williams for the privilege of recording these cases, which are as yet unpublished, and for the help and suggestions that he has given me in our correspondence during the past few months. This makes six cases that Dr. Williams has had under his observation.

CASE IV.—*Female, aged forty-four years. Six months before operation a small tumor was discovered in the left upper quadrant of the abdomen. The subjective symptoms were those of indefinite intestinal disturbance and constipation. The tumor was fixed and did not move on respiration. The omentum overlay the growth, but the intestines were not carried forward on the anterior surface of the tumor. Operation showed the tumor originated in the retroperitoneal space, just below the splenic flexure of the colon. Death six months after.*

Female; white; aged forty-four years. The family history and her past history are both good. She is the mother of nine children.

She was somewhat spare of build, but her general health had been perfect. In June, 1903, she began to suffer from some flatulence after eating, and constipation. Her family physician was called in and discovered a small lump or mass to the left and above the umbilicus. The mass rapidly grew and interfered decidedly with the functions of the bowels, producing obstinate constipation. The tumor prevented her from standing erect. She had never had pain, nausea, or vomiting, and practically no loss of flesh or strength. A physical examination made upon November 11, 1903, revealed a tumor as large as a croquet ball, which could be easily outlined through the thin abdominal wall. The tumor was fixed and was uninfluenced by respiration. There was no evidence that any portion of the intestines lay between the tumor and the abdominal wall.

An exploratory operation upon November 13, 1903, revealed a tumor adhering to the omentum and through it to the anterior abdominal wall. When the adhesions were broken it was found that the descending colon lay to the left of the growth and the small intestines to the right. There were many large veins on the surface of the tumor.

The tumor sprang from the retroperitoneal space to the left of the point where the transverse colon with its mesocolon crosses the duodenum. The mesocolon was not involved.

The situation of the tumor and the condition of the patient were such that the extirpation of the tumor could not be undertaken. The patient recovered from the operation and returned home in two weeks. She died six months after the tumor was first noticed.

Although there was no microscopic examination of the tumor, there can be do doubt that the growth was primary in the retroperitoneal space, and that it was malignant in character. These two facts render it almost certain that the growth was sarcoma.

The case is interesting because the tumor originated in such a position that it did not dissect up the layers of the mesocolon and carry the bowels forward on its anterior surface. It grew in such a manner that the omentum was the only structure pushed forward by its growth. In its insidious onset, in the production of indefinite digestive disturbances, and in its quick course and absence of cachexia until the growth was large enough to seriously interfere with the abdominal organs, the tumor closely follows the type of retroperitoneal sarcomata of the upper left quadrant.

If Dr. Williams had not operated so promptly, it is probable that in due time the tumor would have dissected up the mesocolon and carried the colon forward on its anterior surface. It is probable that this did occur before death, but as there was no autopsy no information can be given upon this point.

CASE V.—*Female, aged three years. History of constipation and vomiting for several months; decided cachexia; examination showed a large tumor occupying the left side of the abdomen; enlargement of*

the abdominal veins and œdema of the left leg. The mass was immovable on palpation and upon respiration. It was flat upon percussion, except for an area of tympany over the right edge, which was shown on operation to be the colon. Operation: The tumor sprang from the anterior surface of the left kidney and pushed the descending colon over to the right; extensive central colloid degeneration; death in twenty hours after operation.

R. P., female, aged three years. Family history was very good. The child had never been strong. For several months there had been digestive disturbance, constipation, vomiting, loss of weight, and inability to walk. The child received no regular medical attention until the end of January, 1904. Examination at that date showed the presence of a large tumor occupying the left side of the abdomen, from the costal border to the iliac crest and extending to the right of the umbilicus. The veins on the surface of the abdomen were enlarged and the left leg was œdematous. On palpation the mass was firm and appeared to be solid. It was flat upon percussion, except over the right edge, where there was tympany. The growth was immovable upon palpation, and did not move during respiration. The child was anæmic and cachectic. Examination of the urine showed a specific gravity of 10.20, no albumin, no sugar, and no blood.

Dr. Williams operated at once, and I quote the description of the operation from his report:

"An incision was made on the left semilunar line five inches long. The omentum was not adherent and there were no adhesions. The peritoneum could be moved over the growth, which was the size of a small child's head. The descending colon was pushed over to the right, and the mesocolon rested upon the mass and was loosely adherent to it. The peritoneum over the presenting surface of the tumor was incised and stripped up. There were enlarged veins over the surface of the growth. On palpating the exposed portion of the tumor a sense of softness was obtained, and an exploring trocar was thrust into the growth and drew off some drops of gelatinous fluid. The incision was enlarged and a quantity of grumous colloid material escaped. The interior of the tumor was broken down with the finger, and this greatly reduced the size of the growth and made the further steps of the operation easier. The tumor was now enucleated by blunt dissection. The tumor was in this way separated from the colon and mesocolon and then from the left abdominal walls. Its base was found to be adherent to the capsule of the left kidney on its anterior surface, and it was necessary to remove the kidney with the tumor. The spleen, pancreas, and stomach were free. The tumor was not adherent to the posterior abdominal wall.

"Hemorrhage was checked by the free use of ligatures. The circulation of the descending colon was not disturbed, which was satisfactorily demonstrated after completing enucleation. Deep

drainage was provided and the abdomen closed. Dissection of the mass showed that the tumor was attached to the capsule of the kidney. The kidney was easily shelled out of its capsule, and the renal tissues were not involved, except in one small area, the size of a hazelnut. The suprarenal body was not involved."

The child stood the shock of the operation fairly well and quickly recovered from the anæsthetic. She showed symptoms of shock during the following night. Pulmonary œdema developed, and the patient died twenty hours after leaving the operating table. A microscopic examination of the tumor made by Dr. H. F. Harris, of Atlanta, showed that it was a spindle-cell sarcoma with colloid degeneration. No kidney tissue was found.

During the four years that have elapsed since my first review of the literature of retroperitoneal sarcoma nothing new has been contributed to the diagnosis and symptomatology. However, many new cases of great interest have been recorded in current literature. These cases have been studied with greater care than was formerly the custom to give to such tumors, especially with regard to the physical signs and the relation of the colon, small intestines, and stomach to the growth. Witzel's observations upon the relation of the hollow viscera to tumors originating in the retroperitoneal space have been accepted as one of the most important diagnostic signs of this condition.

In general, it may be said that the attention given to such tumors is beginning to assume the importance that they deserve, and the physical signs and symptomatology are recognized as forming a definite symptom-complex.

Rudolf Goebell has contributed, perhaps, the most important article of the past four years upon solid tumors of the retroperitoneal space. He considers the subject of lateral retroperitoneal tumors of all varieties, and includes in his list 30 cases of sarcomata. His series contains 10 cases, to which I did not have access. The remaining 20 were included in my first series. He does not report any new instances of the condition, nor do his conclusions add anything new to the diagnosis or symptomatology. His paper is classical in its thoroughness, but is confined to the consideration of lateral tumors and is consequently limited in its scope.

M. L. Harris and M. Herzog have contributed an excellent article upon the tumors of the mesentery proper, that is, those that grow in or around the lymphatic glands situated between the layers of the mesentery. Such tumors have little in common with solid tumors of the retroperitoneal space, and none of the 57 cases which they have collected are available for my list.

Howard J. Williams reports 3 new cases of retroperitoneal sarcoma, which are included in my second series. He states that he has collected 11 new cases, but on referring to the authorities given, it was discovered that 9 of these were tumors originating in the

mesenteric glands, and, therefore, cannot be considered retroperitoneal, as the term is generally used. The tenth case (reported by R. C. Smith) was included in my second series, and the eleventh case to which he refers could not be found in the reference given. Dr. Williams gives an exceedingly interesting review of the subject, especially the operative treatment of the condition. He has seen more cases of retroperitoneal sarcoma than have been reported by any one American observer. I wish again to express my deep obligation to him for the privilege of reporting Nos. 4 and 5 of the new cases recorded here for the first time.

Otto Hartman reports a new case of upper central retroperitoneal sarcoma, which is referred to at length as Case 69 of the new series.

R. Douglas reports 1 new case and gives a short excellent review of the symptomatology and diagnosis of such tumors.

In addition, new cases have been reported by W. E. Hughes, John McLachlan, R. C. Smith, and J. M. Withrow.

My first series contained 61 cases. The second series contain those that have been recorded in current literature since January, 1900, and those that were overlooked or to which I had no access at the time of writing my first paper, and amount to 30 in all.

The first series together with the second series and the 5 new cases amount in all to 96 cases, upon which the following conclusions are based:

AGE. The combined table of 96 cases show that retroperitoneal sarcoma is more frequent in the first, fourth, and sixth decades. 71 per cent. occurred in the third, fourth, fifth, and sixth decades. The oldest case was a woman of eighty years (Case II. of my own series), the youngest was a baby under a year, reported by C. A. Martin (Case 38).

Age.		Age.	
0 to 10 years	14	51 to 60 years	21
11 " 20 "	4	61 " 70 "	5
21 " 30 "	11	71 " 80 "	4
31 " 40 "	15	Not given	5
41 " 50 "	16		

SEX does not appear to be a predisposing cause. The combined tables show 44 males and 46 females. In 6 the age was not recorded.

POSITION. The whole list of cases have been reclassified as to their position, with rather more elaboration than in the original report. The table is as follows:

Central	19	Left lumbar region	12
Upper central	6	Left iliac region	5
Pelvic	6	Left central region	1
Right lumbar region	18	Lumbar region, side not given	1
Right iliac region	12	Whole abdomen	1
Right central region	6	Not given	3

Total central tumors	31
Total lateral tumors	56
Total right-sided tumors	36
Total left-sided tumors	19

MULTIPLE TUMORS.

2 tumors, both left upper region	1	2 tumors, left upper and pelvic	1
2 tumors, left upper and right lower	1	3 tumors, in region of kidney	1

ORIGIN. It is very hard to determine the point of origin with any degree of confidence. It is perhaps fair to assume that a tumor composed of round, fairly separate nodules, and consisting of small, round cells, had its origin in the lymphatic glands. On the other hand, spindle-cell sarcomata probably spring from fibrous tissue.

In some instances it is fairly easy to determine the point of origin, as when the tumor grows from the periosteum the capsule of the kidneys or the sheath of the great vessels. The following table is more condensed and simpler than the one in the original paper, and the number of cases classified as doubtful is much larger:

Lymphatic glands about spine	5	Periosteum of ilium	1
" root of mesentery	6	Connective tissue of retroperitoneal space	6
" root of mesocolon	4	Sheath of great vessels	2
" on promontory of sacrum	1	Wall of retroperitoneal abscess	1
Capsule of kidney	10	Connective tissue of pelvis	1
Periosteum of spine	7	Uncertain	52

Naumann suggests that the tumor in his case originated in the Neben-Körper of Zuckerkandl.

MORBID ANATOMY. The physical characteristics of the tumors in the new cases accord very closely with the description of the gross morbid anatomy of the retroperitoneal sarcoma given in my original paper. In the early stages the tumor is hard or elastic, usually round, and very often nodular. It is well encapsulated and white and glistening. The tumor is very prone to degeneration. This degenerative process usually commences in the centre and often progresses to such a stage that the tumor becomes cystic. The degeneration does not always commence in the centre of the growth, but may occur at any point in the periphery, giving rise to softer areas that may be distinctly felt through the abdominal wall. The combined list shows that in 29 cases the tumor was so degenerated as to form a cyst. In almost every one of the remaining cases there were areas of softening in some part of the tumor. Usually there is considerable hemorrhage in the tissue of the growth, and the fluid of the cyst is often described as brown and sanguineous.

The combined tables of the variety of sarcoma in 64 cases are as follows:

Small round cell	13	Myxosarcoma	1
Large round cell	2	Angiosarcoma	1
Polymorphic	9	Myxosarcoma cavernosus	1
Spindle cell	21	Giant-cell sarcoma	1
Lymphosarcoma	6	Alveolar sarcoma	2
Fibrosarcoma	3	Variety not stated	4

In the second of my own cases and in those of McGraw (Case 28) and McLachlan (Case 75) microscopic examination showed that the tumor contained unstriped muscle fibre. This is easily explained by the fact that bands of unstriped muscles traverse the retroperitoneal space, and are, therefore, easily included in tumors arising in this region.

Metastasis occurred in 31 cases, and the following table gives the different localities of the secondary growths:

Liver	11	Lungs	8
Spleen	8	Skin	3
Kidneys	8		

Lymphatic glands, scrotum, adrenals, muscle, mesentery, mesocolon, pleura, heart, bone, cord, dura, neck, 1 each.

Symptomatology. The onset of retroperitoneal sarcoma is insidious, and the symptoms are not characteristic until the tumor has become large enough to be detected by physical examination. The growth generally manifests itself first by signs of pressure upon some of the structures in the peritoneal cavity or retroperitoneal space. The character of these symptoms can best be described by considering the results of pressure produced in the different regions of the abdomen.

In tumors developing in the *upper central region* the most common symptoms are those of gastric disturbance. In the early stages these are usually indefinite in character and consist of discomfort after eating, vague pain, and nausea. As the tumor enlarges pain is more severe and vomiting occurs.

In 3 of the cases (Cases 65, 68, and No. III. of my own series) there were crises of abdominal pain with vomiting much resembling cholelithiasis, but without tenderness over the gall-bladder, jaundice or other symptom of gallstones. The tumor in every case was in the upper central region and displaced the stomach downward and backward.

In Case 69 the sarcoma grew behind the lesser curvature and cardiac end of the stomach and by its pressure diminished the capacity of that organ, so that the patient experienced a feeling of satisfaction and loss of appetite after taking a very small quantity of food. He had dysphagia due to pressure upon the cardiac end of the œsophagus. The hydrochloric acid of the gastric contents was diminished, and this fact, combined with the presence of a mass, led to the diagnosis of gastric cancer, and to the operation which revealed a retroperitoneal sarcoma growing behind the stomach.

When the tumor originates in the *right or left upper quadrant* pressure symptoms are not pronounced, and consist chiefly of digestive disturbances of the indefinite character already mentioned, nausea, vomiting, and vague abdominal pain.

The growths in the *lower half of the abdomen* give earlier signs of

their presence and produce pressure symptoms which are more severe and more easily localized.

In tumor of the *lower right or left quadrant*, the result of interference with the veins and nerves of the iliac fossæ, are œdema and neuralgic pains in the foot and leg of the same side. Occasionally this pain is very much localized, especially in the early stages of the growth.

In Rogowski's case (Case 78) the first symptom was pain in the right foot, most marked in the heel and gradually spreading over the whole leg. The tumor grew from the right iliac fossa. Keresztszeghy's case in the first series (Case 21) was strikingly similar. The tumor was in the left iliac fossa and the pain was at first very severe and localized in the left foot, and gradually spread over the leg.

In Case 80 of the second series there was contraction of the adductor and flexor muscles in the leg on the same side, accompanied by severe pain. The tumor grew from the right iliac fossa.

Ellis (Case 11) reports the case of a boy, aged seven years, who had œdema of the left lung and of the left side of the face. The tumor surrounded the left kidney, but did not involve it.

In Osler's case (No. 44) there was polyuria without sugar, and the tumor grew in the median position. It seems probable that the symptoms in both of these cases were due to pressure upon the sympathetic system of the abdomen.

Femoral phlebitis occurred three times.

In Lunier's case (No. 27) blood was passed from the urethra, and on one occasion a piece of tissue was discharged through the same channel. Microscopic examination showed that this was from a lymph gland, and a diagnosis of tumor of a retroperitoneal lymph gland was made. Autopsy revealed a retroperitoneal sarcoma that had perforated the bladder.

Ascites may occur, but is not frequent. Hydronephrosis is also rare, and occurred in but 3 cases.

Tumors of the *pelvis and lower central abdomen* produce early and definite pressure symptoms, as would be naturally supposed. Difficult micturition is one of the earliest and most common manifestations of retroperitoneal sarcoma in this region. It varies from frequent urination in the early stages to the complete obstruction of the neck of the bladder in the later stages.

Pelvic tumors usually produce constipation, which may amount to intestinal obstruction. Other cases, especially in the earlier stages, have persistent diarrhœa.

If the tumor encroaches upon both iliac veins, there will be œdema of the genitalia and both legs.

Occasionally, if the tumor originates in such a position that it does not press upon any of the structures of the peritoneal cavity and retroperitoneal space, there are no pressure symptoms, properly

speaking, but merely evidences of interference with the function of the digestive tract. In such cases pain and œdema and the other signs of pressure appear later in the course of the condition after the tumor has attained sufficient size to encroach upon the neighboring structures.

PHYSICAL EXAMINATION. In the early stages the physical signs of retroperitoneal growths are those of a deep-seated abdominal tumor, concerning which little can be determined by palpation. Such tumors are rarely observed in their early stages, since their symptoms are so vague at the onset that medical advice is not sought until the tumor has grown to such a size that it is plainly perceptible to the patient himself.

The insidious onset of retroperitoneal sarcoma is a real source of danger, since by the time that the tumor is discovered it has grown to such a size that an operation is exceedingly difficult or impossible, and this is probably the reason why the results of operative treatment are decidedly unsatisfactory.

As the tumor enlarges, its retroperitoneal position can usually be determined by the signs that are becoming definitely recognized as peculiar to growths originating in the retroperitoneal space.

The relation of the colon and other hollow viscera to the tumor is by far the most important part of the examination in determining whether or not the growth originated behind the peritoneum. Since Witzel first called attention to the characteristic relation of the stomach and bowel to retroperitoneal tumors, many writers have verified his statements.

The conclusion of my first paper as to the relations of the colon to retroperitoneal tumors proper agreed substantially with those of Witzel, except that several of the collected cases demonstrated conclusively that the transverse colon may be displaced forward by retroperitoneal tumors in the median position, although Witzel claimed that this could not be the case. Two cases reported here for the first time illustrate the importance of careful study of the relation of hollow viscera in the diagnosis of retroperitoneal tumors.

The most important systematic observations that have as yet been made upon the relation of the colon to abdominal growths are those given in the recent classical paper by W. L. Harris entitled "The Relation of the Colon to Intra-abdominal Tumors."[1] Dr. Harris confirms the conclusions of my first paper, but has carried the subject farther, and has included in his observations tumors that are not of retroperitoneal origin.

If the colon is carried forward upon the anterior surface of the tumor, it is proven almost beyond doubt that the tumor originates in the retroperitoneal space.

[1] Journal of the American Medical Association, February 18, 1899.

The stomach is displaced outward and to the left by upper central tumors, and coils of small intestines may be found upon the anterior surface of tumors that sprung from the root of the mesentery and grew up between its layers. However, the relation the stomach and small intestines bear to retroperitoneal tumors is not as characteristic as the displacement of the colon to which reference has just been made.

The following is a classification of the relation of the colon to tumors originating in the various regions of the retroperitoneal space:

1. *Upper central* or *median tumors* sooner or later dissect up the peritoneum until they reach the transverse mesocolon, and then, as they enlarge and grow between its leaflets, the colon is carried forward upon the anterior surface of the mass. The bowel usually runs across the anterior and lower surface and curves slightly downward, with the convex of the curve toward the umbilicus. But it may run along the anterior and upper surface, as in Case III., where the transverse colon occupied the sulcus between the tumor and the liver (Fig. 2).

If the tumor is not exactly in the median position, but grows a little to one side or the other of the median line, the transverse colon may cross the anterior surface of the growth diagonally. (See Fig. 1.)

2. *Lateral tumors* carry the ascending or descending colon forward upon their anterior and inner surface in the same manner. Then the colon curves slightly inward with the convex portion of the curve toward the umbilicus. Here, also, under some conditions depending upon the direction of the tumor's development, the colon may cross it diagonally. The important fact is that the tumor has grown between the layer of the mesocolon and has carried the large bowel forward on its anterior surface. This cannot occur with tumors originating within the peritoneal cavity.

This relation of the colon to retroperitoneal growths is not characteristic of retroperitoneal tumors proper in the accepted sense of the term, as was insisted upon in my first paper. It is seen in tumors developing in the kidneys (Fig. 3), in the adrenals or in the accessory adrenals, in the remains of the Wolffian ducts, in pancreatic cysts, in abdominal aneurism (Fig. 4), and, in fact, in any growth originating in the retroperitoneal space, using the term in its broadest sense.

Harris states that in 95 per cent. of 34 cases of pancreatic cysts the colon was carried forward and downward, but the relation of the colon to pancreatic cysts is not as characteristic as its relation to retroperitoneal growths developing farther down, since the pancreas lies almost entirely above the transverse colon; consequently the colon will not cross a pancreatic cyst as far up upon the surface of the tumor as it would in the case of a retroperitoneal tumor originating in the middle of the retroperitoneal space.

A true retroperitoneal tumor may be so situated as not to affect the colon. In the growths originating in the upper central or upper left portion of the retroperitoneal space, the stomach and not the colon is displaced. In such cases the stomach is pushed forward and to the left.

In tumors growing from the attachment of the mesentery and separating its layers, the small bowel surrounds the growth like a crown and may even cover it completely, so that there is tympany in front of the mass, and as the tumor extends laterally and reaches the abdominal wall in the flank, there will be dulness in this region with the tympany in front, so that the whole picture suggests abdominal effusion. In several of such cases attempts have been made to draw fluid with the aspirator.

The presence of the colon between the tumor and the anterior abdominal wall can best be demonstrated by inflating the bowel with air through the rectum.

In the early stages the tumor is firm in its consistency and is often nodulated or knotty, especially when it originates in the retroperitoneal lymph glands. The tumor may be very hard, but the term elastic is used with striking unanimity by the various observers in describing its physical characteristics.

In Case I. the large and firm spindle-cell sarcoma originated in the upper central region, possessed this peculiar elastic consistency, and resembled the liver so closely on palpation that the growth was supposed to be the liver enlarged from passive congestion.

In Case III. the tumor was distinctly elastic without fluctuation, except in one small area.

In the case reported by Jacoby (No. 15) a thrill was felt over the mass resembling that often observed in an echinococcus cyst. The autopsy shows a sarcoma with multiple area of degeneration.

Although in the earlier stages the tumor of retroperitoneal sarcoma is hard or elastic, there is a distinct tendency to degeneration, which occurs rather earlier in the course of retroperitoneal sarcoma than other solid tumors of the abdomen. This tendency to softening is distinctly characteristic of retroperitoneal sarcoma, and is practically the only point in the diagnosis by which it can be distinguished from other solid malignant tumors of the retroperitoneal space.

The degeneration is usually described as hemorrhagic, and, unless the growth is removed in its first stage by the surgeon, the autopsy reveals, in a majority of cases, a central cavity filled with a cheesy, brownish fluid containing old blood pigments, or the evidences of recent hemorrhages.

In 30 of 96 cases the tumor was so degenerated that it had become practically a cyst, of which the walls were formed by the remains of the tumor mass, and the centre was filled with the fluid contents described above.

In 12 of the cases fluctuation of the mass as a whole was obtained before death, and in many more small softened areas were observed, although the rest of the tumor remained firm and hard.

The tumor is usually immovable, owing to its deep position and broad attachment. However, in 15 cases the tumor could be moved on palpation, and in 6 it moved on deep inspiration. When the mass was affected by the movement of the diaphragm, the growth was most often in the right lumbar region, and the movement is probably explained by attachments to the liver or the pressure of that organ upon it. But there may be movability synchronous with respiration in tumors which originate in other localities. Stiller reports such an instance in which the mass was in the upper left quadrant of the abdomen. In Witzel's case the tumor moved with deep respiration and sprung from around the lumbar vertebræ. R. Johnson reports a tumor that sprung from the left lumbar region, which moved on respiration. In a case reported by S. W. Morton there were two tumors, one in the lower right quadrant and one in the splenic region, that were influenced by respiration, probably on account of adhesions between them and the abdominal wall. Willutski reports a sarcoma occupying the left side of the abdomen, which sprang from the periosteum of the spine, which was freely movable, and Lossen records an instance of a sarcoma springing from the capsule of the right kidney, which was extraordinarily movable on palpation.

The growth of the tumor is decidedly rapid. In 58 cases in which the duration could be definitely determined, the average length of the time from the beginning of subjective symptoms to operation or death was eight and a half months. The shortest case reported by Chassagne ran thirty-two days. McGraw reports a case of a man who had had a slowly developing tumor in the abdomen for five years, but in which the increase in size was very rapid in the last six months of life. It seems possible that the period of rapid growth in this case represented the true duration of malignancy. In Case I. we noticed no change in the tumor during the last fifteen months of life, although its development before this time had been rapid and occupied a space of about two months. Case I. is also remarkable for the lack of cachexia, and for the very slight influence that the sarcoma had upon the patient's general health and strength. Indeed, her death was due to other causes than malignant tumor. It is probable that the patient's advanced age prevented the rapid tissue changes that would have occurred in a similar growth in a younger person.

TERMINATION. The termination is usually death from exhaustion, unless there is surgical interference.

Case 49 died in collapse from rupture into the stomach of a sarcoma that had become cystic from central degeneration.

In Case 81, the tumor ruptured into the small intestines.

Case 88 died from rupture of an enlarged vein upon the surface of the tumor.

In three instances death resulted from the rupture of the softened tumor in the peritoneal cavity.

Tapping was resorted to in 5 cases. Case 65 gave a few drops of blood. Case 80 gave yellow fluid, with pigmented round cells and spindle cells. The tumor was a round-cell sarcoma that sprang from the periosteum of the spine. Case 90 was tapped three times, and each time gave a small amount of clear serous fluid. Case 39 gave viscid blood. Aspiration offers some aid in differentiation between cysts and solid retroperitoneal tumors, but it is questionable whether the measure is justifiable, in view of the fact that running a needle through the peritoneum into the tumor must be attended with some risk, and that the only hope of recovery in any malignant retroperitoneal tumor lies in operation.

In a certain number of cases wasting and anæmia appeared slowly and comparatively late in the course of the tumor's development, but, taken as a whole, cases of retroperitoneal sarcoma present the same degree of emaciation and cachexia that are characteristic of other malignant tumors.

Diagnosis. The differential diagnosis between solid malignant tumors of the retroperitoneal space and other tumors in the abdominal cavity which might be confused with them, has been fully discussed in my previous paper, and a study of the cases here reported for the first time, and of the additional cases collected from literature, only emphasizes the fact that a positive diagnosis as to the origin of solid malignant retroperitoneal tumors is practically impossible without exploratory incision.

Tumors of the kidneys and pancreas may manifest themselves by the urinary and digestive disturbances peculiar to these organs. New-growths in the adrenals may give more or less definite symptoms of Addison's disease. However, tumors may develop in any of these three organs without characteristic clinical symptoms.

The following case illustrates very well the difficulty of distinguishing between a solid tumor of the kidney and the so-called retroperitoneal tumor proper. The case was one of carcinoma of the kidney, and is clinically identical with a typical case of malignant retroperitoneal growth.

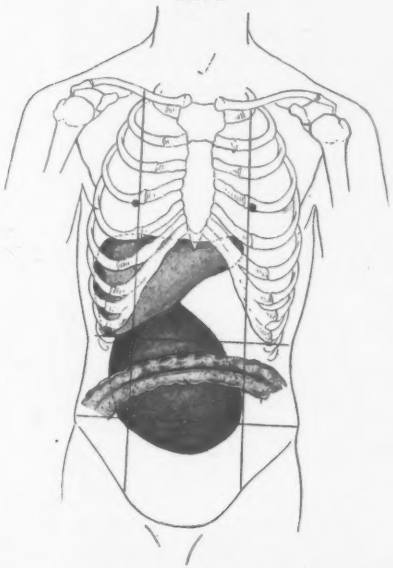
Case VI.—*Woman, aged fifty-five years; rapid loss of flesh and strength for three months and severe pain in the epigastrium; œdema in both legs; a large tumor occupying the right and lower portion of the abdomen; the tumor was hard and slightly movable; the transverse colon ran across the upper anterior surface; death from exhaustion. Autopsy. Large carcinoma originating in the right kidney.*

The patient was a woman, aged fifty-five years, who had been failing rapidly in strength for three months previous to applying for treatment. The only subjective symptom that she complained of

was a severe pain in the epigastrium. There had been no pain in the legs and very little in the lumbar region. About a week before death there was considerable swelling of both legs below the knees. There was no diminution in the amount of urine, which was passed involuntarily and could not be examined. Her bowels were open and there was no symptom of intestinal obstruction.

Physical examination showed a tumor occupying the lower portion of the abdomen. Its upper border was at the umbilicus, the left border extended 9 cm. to the right of the median line. Lower border extended within 2 cm. of the umbilicus, and its right border ran

FIG. 3.



CASE VI.—Carcinoma of the right kidney. The colon is pushed forward and crosses the anterior surface of the tumor.

over to within 3 cm. of the crest of the ilium. The lower portion of the tumor was fairly regular and rectangular in shape. The tumor was hard in consistency. The upper right-hand corner extended up under the liver, but the edge of the liver could be plainly felt and did not appear to be adherent. The tumor was slightly movable on palpation for a distance of not more than 1 cm. in any direction. It did not move on respiration. Running transversely across it about 2 cm. below the umbilicus was a band that, on palpation, appeared to be the colon (Fig. 3). At times tympany could be elicited over this structure, and masses which appeared to be fecal masses, from their consistency and changeability of position, were plainly felt in

it. On the right and left edge of the tumor could be felt vertical bands that were thought to be the ascending and descending colons. At a point a little below and to the right of the umbilicus was a point where indistinct fluctuation could be obtained. The liver was slightly enlarged, extending from the fifth rib 4 cm. below the mid-clavicular line. Several nodules were felt upon its surface, which appeared to be about the size of a cherry; otherwise the surface of the liver was smooth. With the exception of the structure supposed to be the colon, there was nothing between the tumor and the anterior abdominal wall. The flanks were full, but palpation did not give the impression that the right flank contained more than the left.

I am indebted to Dr. W. B. Stanton for the notes upon the autopsy, which was limited to the abdomen.

There was a large tumor originating in the right kidney and extending from the ilium to the costal arch. The abdominal cavity was smooth and contained almost no fluid. The descending colon lay upon its anterior surface. The spleen was not enlarged. The liver was not enlarged, but its right lobe contained one yellow nodule about the size of a quarter-dollar. The stomach and intestines were healthy. The microscopic examination showed that the tumor was carcinoma of the kidney.

The immovability of the tumor and the position of the colon rendered a diagnosis of retroperitoneal growth easy. The fact that a specimen of the urine could not be obtained made it difficult to tell anything of the condition of the kidneys, although it is quite possible that the urine might not have furnished any information. The case was seen only for the last three days of life, and the autopsy was limited and hurried, so that the report is not very thorough, but the case illustrates very well the relation of the colon to tumors of the kidney.

Retroperitoneal lipomata and the rare retroperitoneal congenital cysts may usually be distinguished by their physical characteristics, and tapping would be conclusive. Various rare, solid, non-malignant tumors of the retroperitoneal space have been reported, such as myofibromata and osteoenchondromata. The distinction between them and retroperitoneal sarcomata should be made by the history and course.

Tubercular enlargement of the retroperitoneal lymph glands should offer no difficulty in diagnosis. For a more detailed consideration of this subject, see my previous paper.

Mesenteric cysts present a fluctuating tumor, which lies at first laterally, but which enlarges and comes to occupy the middle of the abdomen, points toward the umbilicus, is freely movable, especially transversely, and rotates upon its axis. It is surrounded by a zone of tympany and has a zone of tympany passing over it.[1]

[1] Moynihan, Annals of Surgery, July, 1897.

Solid tumors originating in the mesentery are very movable, and are distinguishable by this characteristic from the retroperitoneal tumors originating at the base of the mesentery and growing up between its leaflets. In other respects, namely, the arrangement of the small bowel in front of the tumor and the dulness in the flanks simulating abdominal effusion, the two tumors are very similar.

Aneurysm of the abdominal aorta may very closely simulate a solid retroperitoneal growth. When the physical signs characteristic of aneurysm are well marked, such a mistake could hardly be made, but when the aneurysmal sac has reached a great size and has been so nearly filled with organized clots that the usual thrill, bruit, and pulsation are much lessened or entirely gone, such an error may readily occur.

Parker Syms reports a case of aneurysm of the aorta that so closely simulated a solid tumor that an exploratory operation was undertaken.

In the case reported by Phillipson (No. 46), a retroperitoneal sarcoma in the right lumbar region showed a distinct up-and-down pulsation.

One of the best demonstrations that such a mistake might occur is furnished by the following case that occurred in the service of Dr. Musser and under the care of Dr. A. O. J. Kelly, in the medical wards of the University Hospital during the past winter. These gentlemen will, no doubt, publish the case in detail in the future. I will merely refer to the points in the history of the physical examination, which show how closely a large aneurysm of the abdominal aorta may simulate a solid retroperitoneal tumor. I am much indebted to them both for the privilege of publishing the following summary of the history and physical signs:

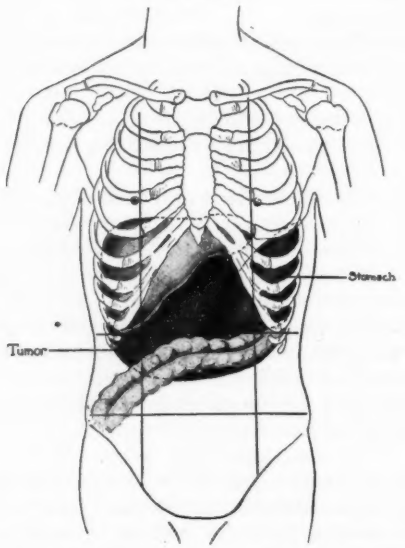
CASE VII.—*White man; aged sixty years. Pain in the whole of the right side referred to the spine and right hip; a large tumor in the centre and right of the abdomen, which was smooth and elastic; the transverse colon overlaid the tumor, and the stomach was pushed out into the left. At this stage the tumor resembled a solid retroperitoneal growth. Later expansile pulsation and bruit developed. Sudden death by hemorrhage from the lungs. Autopsy showed a large abdominal aneurysm, eroding the spine and rupturing through the diaphragm into the lungs.*

The patient was a man aged sixty years. During the past thirty years he had had occasional attacks of pain in the right hip, which had grown worse within the past two years, and had extended over the whole of the right side. Two months previously a prominence was noticed in the epigastrium, which subsequently began to enlarge. The tumor was large and smooth and somewhat elastic. The relation of the tumor to the liver, colon, and stomach is shown in Fig. 4.

When the colon was inflated it overlay the lower portion of the tumor. Inflation showed that the stomach was pushed up and to the

left. The growth could not be differentiated from the liver by palpation or ordinary percussion, but auscultatory percussion rendered it very easy to demonstrate the lower border of the liver. Pulsation was occasionally noticed over the mass in front, but this was not expansile in character, and there was no bruit or thrill. The pulsation was considered to be transmitted from the aorta, and at this period of observation the diagnosis was thought to lie between pancreatic cyst, solid tumor of the retroperitoneal space, or a similar tumor originating in the kidneys. Gradually pulsation spread over the whole area of the mass and was very marked posteriorly in the

FIG. 4.



CASE VII.—Aneurysm of the abdominal aorta. The colon is pushed forward and crosses the anterior and lower half of the tumor. The stomach is pushed forward and to the left. Compare Fig. 1.

right flank, and a bruit developed over the whole tumor, thus forming a very characteristic picture of aneurysm.

The man died suddenly, and the autopsy showed a large aneurysm of the abdominal aorta that had ruptured into the lung.

The case is mentioned because in its earlier stages the growth resembled a solid tumor of the retroperitoneal space so closely that at one time an exploratory operation was seriously considered. The fact that an aneurysm is a retroperitoneal tumor explains the displacement of the colon and stomach that is so characteristic of any growth originating in the retroperitoneal space.

TREATMENT. The only hope for the patient lies in surgical interference and removal of the tumor. Naturally, the earlier in the course of the affection that this is done the better the prognosis. Consequently, the responsibility of making as early a diagnosis as possible lies with the medical man, and hence the importance of including retroperitoneal sarcoma in the list of possibilities when a case is under examination that shows indefinite abdominal symptoms with loss of weight. It is probable that physical examination in deep narcosis after thorough emptying of the bowel might often reveal a retroperitoneal tumor at a much earlier stage than such tumors are generally discovered.

It is not my intention to enter into a discussion of the surgery of retroperitoneal sarcoma. It is sufficient to say, that the only hope of recovery lies in the earliest possible diagnosis and removal of the tumor.

In the 96 cases here reported operation was undertaken 29 times, with 18 deaths and 11 recoveries.

The survival of the patient for two months after operation has been arbitrarily considered a recovery.

CONCLUSIONS. *Frequency.* Sarcoma of the retroperitoneal space is not so very uncommon. In the past few years it has become recognized that the development of such tumors has a definite symptom-complex, and more reference is being made to the condition in current medical literature, with a relatively larger number of reports of cases.

Etiology. The condition is more frequent in the first, fourth, fifth, and sixth decades; 53 per cent. occurred in the interval from the thirtieth to the sixtieth years.

Sex is not a predisposing cause. In 90 cases there were 44 males and 46 females.

In 4 cases there seemed to be a direct relation between an abdominal injury and the development of the tumor.

In 1 case the tumor grew from the wall of a retroperitoneal abscess.

Course. The development of the tumor is very quick. The average interval from the time the growth was first detected to operation or death in 58 cases was eight and a half months.

Position and Morbid Anatomy. The most common point of origin of these tumors is in the lumbar region (30 cases, or 32 per cent.), and the right side is oftenest affected. The next most frequent point of origin is the centre of the retroperitoneal space (19 cases, or 20 per cent.). Next comes the iliac region (17 cases, or 18 per cent.). In 6 cases the tumor grew in the pelvis, and in 4 cases it originated in the upper central region above the level of the umbilicus. The tumor was lateral in a majority of cases (56, or 60 per cent.), and two-thirds of the lateral tumors were upon the right side. The tumor is almost always single. It is usually lobulated and encapsulated, and is hard and firm in the earlier stages, but is very prone

to degeneration. The degenerative process is oftenest hemorrhagic in character, but may be puriform or myxomatous. In a third of the cases degeneration progressed to such a degree that the growth assumed a cystic character.

Metastasis occurred in one-third of the cases. The secondary growths are most often found in the liver and lungs. In many of the cases the new-growth involves the intestines, and in 5 cases a cystic tumor ruptured into the gastrointestinal tract or the peritoneal cavity.

Symptomatology and Diagnosis. Emphasis must be placed upon the fact that the symptoms and signs vary so greatly in accordance with the position of the tumor that a very comprehensive classification cannot be made. The signs most characteristic of sarcoma of the retroperitoneal space may be stated as follows:

The earliest manifestation is the presence of a hard or elastic nodular tumor usually quite immovable, growing deep in the abdominal cavity and giving rise to rather indefinite digestive disturbances. If the mass is placed so as to interfere with the important structures of the abdomen or retroperitoneal space, there may be characteristic pressure symptoms, such as pain and œdema in the legs or genitalia, or obstruction of the urethra or the large or small bowel. As the tumor enlarges, the symptoms of interference with the abdominal viscera are aggravated, and there may be constipation, sometimes amounting to intestinal obstruction, difficult micturition, violent vomiting, or signs of perforation of the bladder, stomach, or bowel.

The point of most value in the physical diagnosis is the relation of the colon and intestines to central and lateral growths, and the relation of the stomach to upper central tumors. The determination of the position of the stomach or the colon in most cases should decide whether or not the tumor is retroperitoneal. When this has been done, the diagnosis is narrowed to tumors of the kidney, adrenals, accessory adrenals, remnants of the Wolffian ducts, tumors of the pancreas, cysts of the pancreas, aneurysms, and solid retroperitoneal tumors in the restricted use of the term.

Perhaps the only sign that is at all characteristic of retroperitoneal sarcoma, and that can be used in distinguishing between sarcomata and other solid tumors of the retroperitoneal space, is the tendency of retroperitoneal sarcomata to degenerate early in their course. When a tumor that is evidently retroperitoneal and that was at first hard and nodular rapidly softens and shows spots of fluctuation, the evidence is strongly in favor of its being a sarcoma springing from the retroperitoneal glands or connective tissue.

An exploratory incision is the only certain means of determining the origin of solid malignant tumors of the retroperitoneal space, and surgical interference offers the only hope of prolonging the patient's life.

The prognosis of the condition is distinctly unfavorable. The chief danger lies in the insidious development and lack of character-

istic signs and symptoms in the early stages of the growth of the tumor. An early diagnosis is imperative, if any benefit is to be derived from surgical interference. It is important, therefore, to recognize that such tumors are not excessively rare and that their development presents a somewhat obscure but still characteristic symptom-complex. Hence it is important to include retroperitoneal sarcoma in the list of possibilities in the examination of cases with indefinite disturbance of digestion and loss of weight, especially if there are signs of pressure upon any of the structures included in the retroperitoneal space.

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TRAUMATIC INTESTINAL RUPTURE, WITH SPECIAL REFERENCE TO INDIRECT APPLIED FORCE.[1]

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THIS subject merits much more conscientious consideration than is usually given to it by surgical authors. I have reference to internal injuries with no manifest external lesions. The degree of injury is no criterion whatever as to the future aspect of the case. Frequently a slight abdominal contusion is followed by great damage to the underlying viscera; while, conversely, a crushing injury to the

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abdominal parietes, severe enough to cause fracture of neighboring bony structures, will not have interfered with the integrity of the abdominal organs. I wish to lay stress on the importance of the absolute necessity of examining carefully all patients suffering from abdominal contusions, and of cautious observation for a requisite period after the time of injury to preclude the possibility of having made a diagnosis of simple abdominal contusion. Then, having assured the patient and his friends of a quick recovery, only to hear later that the patient became suddenly very ill, and in all probability died from a perforative peritonitis.

Relatively speaking, how often we hear of a fracture of the skull or severe injury to the cranial contents having been diagnosticated by the first surgeon in charge as a simple scalp contusion.

Frequency of Segment of Intestine Involved. These injuries are found most often in men and young adults, by reason of their greater exposure to injury. In a study of the statistics of the relative frequency of rupture of the different portions of the intestinal tract, no mention is made in many instances of the exact anatomical location of the lesion.

Jalaguier claims that in all contusions of the abdominal wall, in which the viscera are injured, the digestive tube is involved in one-eleventh of the cases. These statistics are based upon those of Thomas Morton, 234, and those of Coull Mackenzie, 111, making a total of 345, of which 31 concerned the gastrointestinal tract. Chavasse found the ileum and jejunum injured 106 times, large intestine 19, duodenum 7, small and large intestine together 7, and the rectum 1. Curtis, in 113 cases, found the large intestine injured only 4 times. Bryant, in a series of cases, gives the duodenum 2, jejunum 7, and the ileum 10. Croft, in 10 cases, collected between 1873 and 1890, states there were 7 of the ileum and 3 of the jejunum. Maylard recorded 10 cases, of which 6 were injuries of the ileum and 4 of the jejunum. Poland discovered 5 cases of rupture of the large bowel out of 64 injuries to some portion of the intestinal tract. In 40 cases of rupture of the small intestine, only 4 occurred in the duodenum. It will be seen that while the duodenum is firmly fixed in its position, it is, comparatively speaking, rarely injured. It is protected by its thick walls and also by its deep position.

As we proceed in a downward direction to the ileocæcal valve, traumatic rupture becomes correspondingly more frequent. This condition is explained by the greater exposure, especially of the ileum; the mobility of the intestinal coils, and by the gradual attenuation of the tunics of the small intestine. The large bowel is protected in the loin and hypochondriac region. Its contents, which are usually of a semisolid or solid consistency, militate against injury; while we know that the fluid contents in the small intestine play an important role in rupture.

The stomach is rarely injured, on account of its protected position.

Coull Mackenzie, in 111 cases, found the stomach injured only once, and then there was an accompanying injury of the spleen, showing that great force had been exercised.

MECHANISM OF INJURY. Speaking in a general sense, blows directed above the level of the umbilicus are unlikely to cause intestinal injuries. There are certain injuries which should invite suspicion of rupture. Thomas Bryant has well said: "When an individual has been run over, the wheel passing over the abdomen or back, had a kick from a horse, a fall from a height or a crush between two obtuse bodies, there is a great probability of injury to some solid viscus or laceration of the intestine." The usual nature of injuries which produce rupture is shown by the 149 cases of gastro-intestinal involvement collected by Chavasse: 36 were due to kick of a horse; 13 were due to kick of man, blows by clubs, etc.; 23 were due to crushing of wagon wheels. It is obvious that we must first consider the force applied in consideration of the mechanism of the injury. We may classify such force into first, direct; second, indirect.

By direct force I mean that the vulnerating body has been applied in the nearest line to the exposed intestines—that is, against the abdominal parietes. By indirect force, I wish to call attention to an impulse conveyed to the intestines by an impact directed upon the buttocks or the lumbar region. Again, we can classify such injuries in regard to the nature of the applied force into (1) percussion and (2) compression. Strictly speaking, the great majority of cases of traumatic rupture of the intestine are due to compression, although there is only one vulnerating body. A blow is administered upon the abdominal wall; but the rupture is due to the compression between two solid bodies; that is, the vulnerating force and the vertebral column behind or the bony pelvis. This is substantiated by Makin's observation, that intestinal ruptures are found most often in that portion of the intestine which is low in the pelvis. There are undoubtedly ruptures produced in the true sense of percussion—that is, the impulse of the blow might cause violent momentary vibrations in a coil of intestine overdistended with fluid contents, and thus cause a rupture. This supposition is supported by the fact that in the great majority of cases the rent in the bowel is at the convex surface, diametrically opposite the mesenteric border. All cases of rupture produced by indirect force would be effected in this manner.

In a careful search of the literature, I have found only 2 well-authenticated cases of rupture produced in this manner, both of which were published in 1902.

Dr. J. F. Bottomly reports a case where the patient was struck in the back below the left shoulder-blade by an approaching wagon. Operation showed a perforation of the first portion of the jejunum. Westbrook describes a case where a wagon-pole struck a man in

the lumbar region. Autopsy revealed a rupture at the junction of the duodenum and jejunum large enough to admit two fingers.

I wish to report the following case as illustrative of an injnry to the intestine, which was produced in a unique way, and shows the possibility of a force of small degree directed upon the buttocks, capable of producing intra-abdominal laceration.

Mrs. J. F. O., aged twenty-six years, married; previous health good; on July 17th, at 6 P.M., while hurrying into her house to escape a thunder-storm, slipped and fell, striking the ground upon the right buttock. She had just partaken of a hearty supper. No immediate alarming symptoms were noticed, and the patient retired as usual. At midnight she awoke with severe abdominal pains; vomited once. The following day she was seen by her physician, Dr. G. F. Berger, who prescribed opiates and turpentine stupes. The pains increased and the patient rapidly grew worse. I was called in consultation on the morning of the 19th. The appearance of the patient was critical. She had an anxious expression, and complained bitterly of abdominal pains. Temperature, 104.3° F. (rectal); pulse, 140. Manual palpation revealed diffuse abdominal tenderness. There was marked tympany, most noticeable over a limited area in the region of the appendix. Without the history of the injury a diagnosis of appendicitis would have been the most probable. A provisional diagnosis of perforative peritonitis was made, and the patient advised to undergo immediate operation. She was transferred to the German Hospital. Stimulation with strychnine and salt solution enemata.

Operation. Anæsthetic, ether, by the open method. Median incision, four inches long, below the umbilicus. Upon opening the peritoneal cavity there was an escape of cloudy fluid, but no gas. Spider-web adhesions of the great omentum, which were separated, followed by a gush of fluid heavily loaded with fibrinous flakes. Small intestine was greatly distended and of a bluish-black color, and covered with a fibrinous exudate. No collapsed bowel seen. The intestine was now grasped at a fixed point by an assistant, and a search for the perforation made. After a long exploration a sudden escape of gas was noticed deep down in the pelvis. Further examination revealed feces in the peritoneal cavity, and a small perforation, about the size of the little finger-nail, was discovered on the convex surface of what appeared to be the lower portion of the jejunum. The patient was now nearly pulseless, and she was given a subcutaneous injection of salt solution. The abdominal cavity was next thoroughly cleansed by dry sponging, and the perforation in the intestine sutured into the abdominal wound. The lower angle of the incision was left open, and four large gauze drains were placed into the abdominal cavity, two in the direction of the pelvis, and two well up toward the diaphragm. This drainage was supplemented by a tubular drain. The patient was returned to her room in a very

weak condition. She was stimulated with strychnine, camphorated oil, and salt enemata; each administered every three hours, but given at such intervals that the patient had one of these stimulants every hour. The patient rallied, and on the second day was in a fair condition. She recovered entirely from the operation, but the fistula persisted, and the adjacent surface was aroused into a severe dermatitis due to the digestive action of intestinal fluids. I saw her one week after the operation, and she was in good condition. I did not see her again until October 3, 1903, she in the mean time having been treated by Dr. Berger. I found her very much emaciated, literally having starved to death. She had been nourished for eleven weeks per rectum. Food taken by the mouth greatly increased the discharge, and appeared undigested at the opening. The fistula was still patent, in spite of the repeated cauterization with the Paquelin cautery. During the last two days she had two sinking spells. I advised immediate operation as the only means of saving her life; although the wound was unfavorable for operation, on account of the dermatitis.

A second operation was performed October 4, 1903. Two curvilinear incisions around the fistula were made; then a layer of gauze with an opening in the centre was sutured to the wound margins. The opening in the gauze exposed the field of operation and the layer of gauze protected the wound from the surrounding infected skin. The loop of intestine was dissected loose from the abdominal wall. The general peritoneal cavity was next packed off with compresses. The margins of the fistula were trimmed and closed by transverse suturing with two rows of continuous sutures. The first row was passed through all the intestinal coats, the second being Lembert sutures. The line of suture was covered with an omental graft, and the repaired intestine dropped into the abdominal cavity. The external wound was closed without drainage. The patient bore the operation well. The following day she was given peptonoids, two ounces every four hours per rectum. October 6th, peptonoids were given by mouth, and then, October 9th, white of an egg; October 10th, milk; October 11th, oatmeal; October 12th, soft-boiled eggs and bread; October 14th, steak. Her recovery was perfect, and she left the hospital October 23, 1903. I heard from her November 19th. She had gained twenty-five pounds, weighing more than ever before in her life.

Remarks. The history of the cause of the injury was reliable, and that the fall was not severe I can vouch for, as she complained of no soreness in the region of the buttock, nor was there any bruise visible. I did the enterostomy for two reasons, and believe it was the means of saving the patient's life. First, on account of the collapsed state of the patient, requiring rapidity of execution, and, second, because of the paralytic state of the intestine, overdistended with gas, allowing its evacuation as the bowel regained its tone.

The state of the abdominal muscles at the time of injury plays an important role in intestinal injuries. A blow delivered upon a rigid abdomen loses considerable of its force; while an impact directed against the same structure in a relaxed state is transmitted directly to the underlying intestinal coils, and enhances the liability of a rupture. This assertion has been demonstrated beyond a doubt by the beautiful experiments of Eichel.

He first made a series of experiments upon dogs profoundly etherized. The animals were placed upon the back, the extremities being tied and extended. A forcible blow was struck upon the abdomen with a heavy club. The experiments were all negative, laparotomy showing the intestines intact and only slight extravasation in the tissues of the abdominal wall. The same experiments were performed on dogs which had been overfed for two days in advance, but the results were also negative. In another series of experiments the hind-legs were loosened before the stroke. In the first experiment the blow was delivered too high, producing a rupture of the liver. The stomach wall was also the seat of suggillation. In other experiments a hammer was used instead of a stick to produce the trauma, and rupture of the intestine was almost invariably produced. Experiments were also made by striking the lumbar region, the intestines having previously been insufflated with air through the rectum, but no rupture of the intestines was produced. Chauveau maintains that the reverse is the rule. He claims that contraction of the abdominal muscles diminishes the abdominal cavity, and also immobilizes the intestinal coils, and thus favors rupture. This argument, however, should bear no weight, as it stands simply as a personal conviction, or rather an hypothesis, while Eichel's opinion rests upon the firm basis of experimental research. Other conditions may predispose to injury, such as adhesions, alteration of intestinal walls, old reducible hernia, in which the intestinal walls have been weakened by pressure. There has been much discussion as regards gaseous distention facilitating rupture. Longuet, in 1875, claimed that the elasticity of the gas was unfavorable to rupture, while liquid distention favored it. This theory was accepted by Mugnier. The hydrostatic pressure of intestinal fluids is evidently the cause of rupture in those cases produced by indirect force. That gaseous distention would act as an elastic cushion seems plausible.

Pathology. From a pathological standpoint, we can divide these injuries into (1) contusions; (2) rupture: incomplete, complete.

Contusions may be of all degrees, either a simple interstitial ecchymosis or a submucous infiltration; or else there may be an infiltration through the entire thickness of the intestinal coats. The contused surface is more or less rounded or oval, and the long diameter is usually in the long axis of the bowel. The color of the ecchymotic area depends upon the amount of infiltration, and is

usually white or yellow. The surface is denuded and covered by an exudate. Sometimes different areas of contusion are found in the same intestinal loop, or in different loops in the same region. Contusion probably is often produced and causes no untoward symptoms. However, there are cases on record where, after an injury, the patient progressed well for days or even weeks, when there arose suddenly symptoms of a perforative peritonitis, and the autopsy revealed a perforation. At the time of the accident there was a contusion produced, which in time became the seat of an infection; or else, by reason of an interfered-with circulation, a necrosis resulted, which compromised the integrity of the intestine. Thomas Bryant reports 2 cases of delayed rupture. One progressed favorably after the accident until the nineteenth day, when the patient died. Necropsy showed perforation of the duodenum, and an ulcer on the posterior wall of the stomach. In the other case there was a perforation on the fifth day. Autopsy demonstrated a perforation of the ileum four inches above the cæcum. Incomplete ruptures, when one or two of the tunics are torn, in all probability are frequent; however, as far as pathological investigation can be pursued, they are supposed to be rare. In a case observed by Jobert, in 1825, ecchymotic spots were found in the small intestine, and a rupture of the longitudinal fibres of the colon discovered. Poland reports 2 cases of such ruptures in the stomach; in 1 the mucous coat was torn, and in the other the peritoneal coat.

Complete ruptures, when all the tunics are ruptured, are more often brought to view on the operating table and in the post-mortem room. Chavasse, in 149 cases, found this condition 14 times; duodenum, 1; junction of duodenum and jejunum, 3; jejunum and ileum, 10.

Complete ruptures are usually single, but may be multiple, especially following the kick of a horse. Moty claims that there are often two perforations corresponding to the two lateral extremities of the horseshoe. It is a marvellous fact that a contusion of sufficient intensity to cause a complete rupture does not often injure other viscera; for Coull Mackenzie, in 111 cases, only found 2 with accompanying injury to the spleen and liver. The rent in the intestine always occupies the point diametrically opposite the point of the mesenteric insertion. It is sometimes a clean-cut wound, and sometimes the border is ragged and irregular. Leakage after rupture is hindered and even entirely prevented through two factors. We must remember there is no abdominal cavity in reality, the whole of the visceral contents being so closely and equably brought into contact by the pressure of the abdominal muscles and the diaphragm that considerable force is required of the intestinal contents to overcome this. The influence of the pressure of the abdominal muscles upon the intestinal contents is well known clinically; because if an injured coil of intestine protrudes from the abdomen devoid of the intra-abdom-

inal influence, extravasation takes place much more readily. The intrinsic contractility of the intestinal tunics is another inhibitory agent against extravasation. Travers long ago pointed out that in a puncture of the gut, or even an incision two or three lines in length, an eversion or prolapsus of the mucous membrane takes place, and hermetically seals the opening. If the aperture is more than four lines in extent the protuberant mucous membrane is incapable of protecting the perforation. The protrusion of mucous membrane is due to the retraction of the longitudinal fibres. There is also contraction of the circular muscular fibres around the protruded mucous membrane, according to Jobert; thus, temporarily at least, preventing extravasation. Even in extensive complete rupture there is little likelihood of visible fecal extravasation, for Makins, in an exhaustive report of 20 cases, in St. Thomas' Hospital, London, found no appreciable escape of fecal matter.

SYMPTOMS. As this pathological condition is usually the consequence of a severe trauma in the neighborhood of the sympathetic centres, we usually find the classical symptoms of shock. The more serious symptoms soon pass away, unless there is injury of the abdominal viscera or internal hemorrhage, which is denoted by long-continued shock. If there is intestinal rupture, with fecal extravasation, the symptoms of shock merge into those of a general perforative peritonitis. It is difficult to tell where shock ends and peritonitis begins. In an injury produced by a sharp blow, the resulting shock appears more marked than that which follows a severe compression of the abdomen. In cases of contusion or incomplete rupture of the intestine, after the symptoms of shock have subsided, there is some temperature on account of local peritonitis, but not much variation in the pulse. Constipation or diarrhœa may be present and possible blood-stained stools. There is slight pain and abdominal tenderness upon pressure. Such cases, as a rule, follow a favorable course, but may terminate disastrously by reason of secondary perforation internally, or favorably by rupture externally, causing a fecal fistula. In those cases where the contusion is followed by immediate extravasation of the intestinal contents into the general peritoneal cavity, an entirely different picture confronts the surgeon. There is immediate excruciating localized pain. The face is pale, the pupils dilated, respiration superficial, the pulse small, and the temperature subnormal. This complexus of symptoms is soon followed by vomiting. The abdominal muscles are at first fixed and contracted, which is gradually followed by a ballooned abdomen; while respiration becomes of a costal nature. The symptoms now progress rapidly from bad to worse; shallow costal respiration gradually merges into dyspnœa; the anxiety of the patient becomes intense; the eyes are sunken; the pulse thready; the extremities cold and cyanosed, and the patient dies in collapse. These symptoms are the usual outcome in cases of complete rupture. How-

ever, the gravity depends upon the condition of the intestine, whether empty or distended, and also upon the virulence of the infective bacteria. Violent visceral injuries may cause no immediate symptoms. Michaux, out of 100 cases of grave contusions, had 10 cases where patients followed their vocations long after injury, in some of which there was complete laceration. Rioblanc reports 2 similar cases. Poland mentions a case of a child, aged thirteen years, struck upon the abdomen, who walked a mile after the injury, and died thirteen hours later. There was a complete rupture of the duodenum. Holland mentions a girl, aged eleven years, who fell down a flight of stairs. She vomited and then had no symptoms for twenty-four hours, when she died. Autopsy showed rupture of one-half of the jejunum. Chavasse speaks of an injury by kick of a horse at 3 A.M. Patient had severe pain and then felt well until the following night, when he vomited and died in collapse. Post-mortem revealed a complete rupture of the jejunum.

I wish to call attention to retroperitoneal emphysema as an indication which signifies injury to the duodenum or the colon. The loss of liver dulness is an orthodox symptom in many text-books on surgery. This diagnostic resource is by no means infallible, especially if the laceration is limited. While fecal matter is less prone to escape than gas, the latter may escape in very small quantities. Again, we should remember that these injuries usually lie toward the pelvis and the upper quadrant of the abdomen may be isolated by omental adhesions. It is obvious that where a great quantity of gas was liberated in the general peritoneal cavity, the liver would fall away from the abdominal wall, so that a resonant note would be heard but not always, as a highly distended bowel may encroach upon the liver dulness.

Vomiting is considered of great diagnostic importance by many. Trendelenburg and Berndt consider it almost a positive sign of rupture. Berndt claims that in contusion of the abdominal wall without rupture, there may be slight vomiting, it being entirely a reflex process, but in complete rupture peristalsis forces the intestinal contents into the opening, and thus irritation of the cut end of the nerves causes vomiting. While continued interrupted vomiting is by no means absolute evidence of rupture, great weight should be placed on its presence in connection with other corroborative symptoms. The abdominal rigidity soon after injury is ominous. Hartmann, in 37 cases, found rigidity 17 times. He treated such patients by laparotomy, and found visceral injury in each. In the 20 other contusions there was no rigidity; the patients were treated expectantly, and all recovered. Kirstein also dwells upon the importance of this symptom.

PROGNOSIS. The prognosis depends upon certain conditions. An injury soon after a hearty meal, while there is a copious physiological secretion of intestinal juices, would, of course, facilitate

extravasation. The prognosis of wounds which are inflicted in the duodenojejunal region is relatively bad, because they are near the source of secretions and because of the difficulty in dealing surgically with this anatomical region. Horse-kicks upon the abdomen have usually an especially bad prognosis. However, Pech reported 67 cases during the years 1890 to 1897 at the garrison of Luneville, France, with only 2 deaths, treated upon the conservative plan. These statistics seem improbable. Dubujadoux observed 8 contusions from horse-kick, and found intestinal lesions 8 times. The mortality of these injuries in the past has been shocking, and it is only due to the great advance of surgery in the last decade that statistics give a more cheerful aspect.

In 1896 Petry collected 160 cases of rupture of the intestine treated expectantly, of which 149, or 93 per cent., died, and 11, or 7 per cent., recovered. He also collected 42 cases of rupture of the stomach and intestine which had been operated upon; 14, or 33.6 per cent., recovered, and 28, or 66.7 per cent., died. Kirstein collected 18 cases operated upon from the German literature since the publication of Petry's paper, of which 44.5 per cent. recovered and 55.5 per cent. died. D. N. Eisendrath collected statistics of 40 cases of which 19, or 47.5 per cent., recovered, and 21, or 52.5 per cent., died. The prognosis of the future will rest upon an early diagnosis. Immediate operation will reduce the mortality to a minimum. The statistics of Siegel, which I consider of the greatest scientific importance, bearing upon this subject, are as follows: In 532 cases treated expectantly, the mortality was 55.2 per cent.; in 376 cases operated upon there was a mortality of 51.6 per cent. An analysis of these statistics proves that the high mortality is due to late operation, when a general peritonitis had already developed. When the time of operation is taken into consideration, the true status of early aggressive surgery can be conceived, as is proven in a further study of Siegel's statistics.

Cases operated upon first four hours, mortality	.	.	.	15.2 per ct.
" " " " five to eight hours, mortality	.	.	.	44.4 "
" " " " nine to twelve hours, mortality	.	.	.	63.6 "
" " " later	.	.	.	70.0 "

TREATMENT. In all cases of abdominal contusions the prognosis should be guarded, and the patients ought to be kept under careful observation. Upon the least suspicion of rupture immediate laparotomy is the only course to be followed. The statistics of Siegel place this argument beyond question. The surgical treatment of perforating wounds of the abdomen has been decided for all time to come, and a plea for equally decisive measures is made for this pathological condition.

The first laparotomy for rupture of the intestine was performed by Bouilly in 1883, but the case terminated fatally. Moty, in 1889, was successful in the first case on record. The incision should be

made through the linea alba below the umbilicus, notwithstanding the advice of F. Spaeth to make the incision at the point of greatest tenderness. This incision will give a better survey of the abdomen. Usually the injured intestine will lie in close proximity, and if there are concomitant injuries of other organs, they can be most easily reached through such an incision. Upon opening the peritoneum there may be an escape of gas, also exudate containing albuminous flakes. The bowel should be examined methodically from a fixed point until the injured segment is found. I wish again to call attention to the great possibility of multiple rupture, especially in cases due to horse-kick. Small rents should be sutured transversely to the long axis of the bowel. Large lacerations should be dealt with by resection, provided the patient is in good condition. In all cases when there are alarming symptoms, the injured bowel should be anchored in the abdominal wound. Personally, I believe this is a good practice to follow in the great majority of cases. Intestinal drainage is of prime importance where the bowel is paretic and distended. Again, in such injuries, especially if operation is delayed, there is a zone of infection which cannot be rendered sterile by secondary disinfection; hence the great danger of tearing through of the stitches and a resultant secondary peritonitis. In the case I reported in this paper, there was a permanent fistula as a result of the operation, but the patient was in such a desperate condition and time was of such moment that the intestine was sutured to the tissues too near the skin. The proper course to follow, when possible, is to unite the bowel, but leave a small fistula and anchor the segment to the abdominal wall. This procedure has been practised by Bouilly. Verneuil, Farquhar Curtis, Treves, Thomson, and Smith have advised an artificial anus after resection of the bowel. I believe this is unnecessary, as it always insures a secondary operation, while the principles are fulfilled equally well by the procedure of Bouilly, and the fistula will close spontaneously in the great majority of cases. When it is deemed advisable to drop the repaired intestine back into the abdomen, the line of suture should always be re-enforced by an omental graft, as advised by N. Senn. When an expectant course is followed in simple contusion or in cases of ruptured intestine, when for some reason operation cannot be performed, the patient should be placed at rest, with an ice-bag on the abdomen. Feeding by mouth should be prohibited, and nourishment given by rectal enemata. Opium is indicated to diminish peristaltic action of the bowels, and thus inhibit extravasation.

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CASTRATION FOR TUBERCULOSIS OF THE TESTICLE.[1]

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Not many years ago it was generally admitted that a radical operation for extensive tuberculosis of the testicle and epididymis was indicated when only the genital apparatus was affected by the disease, the remaining organs of the body being free. In the *Deutsche Chirurgie*, edited by Billroth and Luecke, will be found Kocher's classical article on the subject. In this he says that the reason for this procedure is the chance of a radical cure, although he admits the possibility of a spontaneous recovery, but which is, in most cases, accompanied by the functional loss of the organ involved. He also points out that a cure without operation is only a possibility, and if the organ with its disease is left intact, with the hope that the affection will finally disappear, the patient is exposed to all the dangers attendant upon suppuration. In other instances the condition demands a radical treatment. In a patient having tuberculosis of one testicle which is left untreated, it is always to be expected that within a short time its fellow will also become invaded by the process. This not only applies to the other testicle, but to the whole organism as well, and if the tuberculous testicle is not removed a metastasis of the process will take place in other parts of the body, usually in the form of a general miliary tuberculosis. From this it would appear that castration is absolutely indicated, and although the prostate and seminal vesicle were enlarged and other subjective symptoms of tuberculous infection of the genital organs were manifest, Kocher noted that these symptoms disappeared in a relatively short time after castration had been done. He even found that suppuration of the spermatic cord and abscesses of the prostate would

[1] Read by title at the French Urological Society, Paris, October 22 to 24, 1903.

oftentimes heal after incision if the diseased testicle were removed at the same time.

König also confirms Kocher's views, and, in his opinion, infection of the prostate and urinary organs is no contraindication to castration, for the reason that the removal of the tuberculous testicle has a favorable action on the disease when located in other parts of the genito-urinary system, as well as upon the general condition of the patient. Southam, Simon, and others are also in accord on this point.

Various are the methods of performing castration, but in most instances, as there is only evidence of the disease involving the testicle and epididymis, the operation has usually been thought sufficient when the organ was simply removed. The technique employed simply consists in a longitudinal incision starting above the spermatic cord and extending down to the lower pole of the testicle. When one or more fistulæ exist, or if the skin should be adherent to the organ, the incision is carried round on both sides, so that an elliptical portion, including the fistulous openings in the scrotum, is removed along with the testicle. After peeling off the scrotal integument the spermatic cord is dissected out from its various coverings and then the arteries, veins, and vas deferens are ligated and the cord is cut through. The ligatures should be left long in order to keep the cut end of the cord from slipping up into the inguinal canal.

The testicle is then dissected out from above downward, and when it is adherent to the scrotal tissues this usually occurs in the neighborhood of its lower pole. When the organ has been removed all hemorrhage should be carefully controlled, the wound irrigated, and, after a final inspection of the stump of the cord, the threads are cut and it is allowed to slide up into the inguinal canal. A gauze wick should be inserted, the parts sutured, and the usual dressings applied.

Von Bungner has pointed out a fact which is well known, that the spermatic cord is often diseased without presenting much evident infection at the time of operation. From this arises the danger that the diseased parts which are left behind in the cord will act as disseminating foci for further tuberculous infection, and, in order to avoid this danger, he recommended a new method which he termed castration with evulsion of the spermatic cord. As in castration, the spermatic cord is separated from the vessels and its surrounding coverings, the vessels are tied off below the external inguinal ring, and then the isolated vas deferens is slowly but steadily pulled upon until it breaks. The piece of vas is removed along with the diseased testicle and epididymis. In his operations, von Bungner was able to extract about four-fifths of the spermatic cord by his method of evulsion, and, according to his statistics, he obtained a cure in 50 per cent. of his cases.

It is quite evident that removal of the vas deferens should be undertaken as far as possible in every case of castration, especially when it is evidently diseased, but the method of evulsion is certainly not devoid of danger. Lauenstein and Helferich pointed out the danger of hemorrhage occurring in the pelvic tissue from the traction exercised on the vessels accompanying the spermatic cord. The first-mentioned authority performed castration with evulsion of the vas in thirteen cases, and in several succeeded in removing quite large portions of the cord with much benefit to the patient, but in two instances such severe hemorrhage arose that it was extremely difficult to control it. Since this time Lauenstein only removes as much of the vas deferens as can be pulled down without exercising traction upon it.

A point which should not be forgotten is that in the method of evulsion the peritoneum can be easily torn, and with the raw surface of the cord the peritoneal cavity might easily become infected. Consequently, the method of evulsion is certainly not devoid of danger, and it also should be remembered that in all probability the diseased spermatic cord will rupture at a point where it is infected by the tuberculous process on account of lesser resistance. If this be true, and there is every apparent reason that it should be so, it would naturally scatter tuberculous material, which would be the starting point for a new dissemination of the disease. For these reasons Shede employs a technique similar to that described by Lauenstein, dissecting the spermatic cord up as high as possible and then ligating it at a point where it appears to be healthy, and, for this purpose, it may be necessary to dissect the peritoneum off the cord to a certain extent. It is evident that in this operation, as in others, the spermatic cord is not always removed beyond the point of disease, and, consequently, the affection still remains in the intra-abdominal portion of the vas which is left behind.

The length of the spermatic cord has been estimated as 32 cm. by König, who also resects the vas deferens under the control of the eye, and he has been able to remove as much as 25 cm.; von Bungner removed four-fifths of its entire length, which means practically about 25 cm., thus leaving from 7 cm. to 8 cm. of the cord, which in all probability was diseased.

Now, supposing the seminal vesicle or the prostate is affected by the disease, if it cannot be denied that the removal of the testicle has a favorable influence on the process, it must also be said that it certainly is insecure as regards the prognosis, especially when the tuberculous process within the organ is advanced, and, therefore, simple castration also must be considered insufficient. The involvement of the other genito-urinary organs in a case of tuberculosis of the testicle should always be admitted as more than probable, even when the spermatic cord appears so be perfectly intact; and von Bungner, in his paper, laid stress upon the fact that tuberculosis of

the urogenital apparatus does not extend in continuity, and that occasionally the orifice of the vas deferens may be diseased, yet at its middle it may be healthy.

König has reported a case in which he found a spindle-shaped thickening at the external inguinal ring extending up the inguinal canal, which proved to be a tuberculous infection, although the spermatic cord seemed to be quite healthy. He points out the fact that the points of election for the development of the tuberculous process are where bends or curves take place in the canal.

The removal or direct local treatment of the infected seminal vesicles or prostate is most advisable, but these organs, unfortunately, are most difficult of access, and that to reach them is a most arduous undertaking is demonstrated by the numerous techniques that have been described.

The procedure described by Zuckerkandl is too severe to combine at the same time with castration, and resection of the vas deferens had better be done at a later date, when the patient has recovered from the operation of removal of the testicle.

The diseased parts are reached by the perineal route, a curved incision being made between the scrotum and anus. The posterior wall of the bladder is exposed and the prostate and seminal vesicles are reached after the connective tissue covering the latter has been opened. As numerous bloodvessels are to be found here, the hemorrhage must be controlled before proceeding, although this is very often a most difficult thing to do, on account of the depth of the parts in which one is working.

The question of hemorrhage has deterred many surgeons from selecting the perineal route, and even so great an authority as König advises against its use, suggesting another technique, which avoids this difficulty, using the sacral route, according to the method of Kraske, for resection of the rectum. The operation is preceded by several days' preparatory treatment of the patient, principally to thoroughly empty the intestine. The patient receives only liquid diet and the bowels are thoroughly emptied daily by castor oil and enemas.

The technique of the operation consists in making two longitudinal incisions, beginning on each side, 2 cm. from the median line at the highest point of the anterior border of the anus, the patient being in the lithotomy position, and carried downward midway between the anus and tuber ischii to the fourth or fifth sacral vertebra. After control of the hemorrhage, the incisions are deepened until the fascia pelvis parietales is reached. The space between the anus and tuber ischii is filled with cellular tissue, in which the inferior hemorrhoidal veins pass, supplying the external sphincter of the anus. There are, however, sufficient anastomoses present, so that there is no danger in cutting and ligating these vessels. The pelvic fascia being exposed, a third incision is made transversely

over the sacrum down to the bone, which connects the two lower ends of the incision. The sacrum is then separated between the fourth and fifth vertebra, which is at about the level of the seminal vesicle.

In order to accomplish this a chain saw is passed through the fourth sacral foramen and the bone sawed through. At this point of the operation it should be remembered that severe hemorrhage may take place on account of section of the middle sacral artery and vein, consequently they should immediately be ligated before the operation is proceeded with.

A flap containing the soft parts and bone has now been formed and is then turned upward and the pelvic fascia is incised on the left side of the rectum, the gut being pushed over to the right. When this has been accomplished the structures to be reached are exposed and the posterior part of the bladder and prostate can be seen. On each side of the latter organ the vasa deferentia may be found, running downward to the point where the seminal vesicles are situated.

Each seminal vesicle is covered by a capsule of a fibromuscular nature, deprived almost completely of any blood supply on its posterior aspect, and, consequently, the capsule may be incised and the seminal vesicle peeled out without any danger of hemorrhage.

It is quite impossible to injure the bladder or the urethra at this point, and it is also fairly easy to remove the entire remaining part of the vas deferens up to the point where it enters the prostate. If thought necessary, the seminal vesicle on the other side may be removed, and should the prostate be found diseased the cheesy foci can be cleaned out with the curette. The parts are then plugged with iodoform gauze and the wound can be closed, only one long tampon being left protruding through the incision, which may be removed on the fourth day. The wound may also be left open for the purpose of local iodoform treatment, but a secondary suture does not give such brilliant results.

As to the after-treatment, it consists in confining the bowels for four or five days and the internal administration of tincture opii in sufficient quantity is indicated during this time, after which the bowels may be opened.

In a way this operation presents evident advantages, principally from the fact that the field of operation is easily reached and all the steps are under the control of the eye. The structures to be attained are not very deeply seated when this method is employed, severe hemorrhage is avoided, and the parts easily drained. The two methods just described are probably the best, but there are many others, principally those of Roux, Villeneuve, Guelliot, Rydygier, and others, that I should like to discuss were the limits of this paper sufficient to permit of it.

Unless the patient is in fairly good constitutional condition, such prolonged operation can hardly be advisable, and that this has also

been so considered by other surgeons is well demonstrated from the fact that attempts have been made to treat the diseased parts by means of iodoform-glycerin injections. Von Bungner experimentally investigated upon the cadaver to what extent injections made directly into the lumen of the vas deferens might be pushed. He injected iodoform-glycerin into the lumen of the spermatic cord after section in both directions, and found that the entire genital tract from the epididymis to the urethral orifice was filled with the solution. Some of it ran out through the urethra. The seminal vesicles were filled, but contained a certain amount of the injected fluid. The liquid came in contact with those parts of the vas deferens which are usually involved in the tuberculous process, as well as the intracanalicular parts and the mucous membrane, both of which become involved during the progress of the process.

It was thought that by this method a cure might result without operation in those parts remaining after castration, but the iodoform treatment might also be employed without having done castration in cases where the tuberculous process is so far advanced that it cannot be eliminated, even by the removal of the entire urogenital tract. Under these circumstances this treatment will relieve the suffering in the later stages of the disease, and it also may be indicated in the very early stages of tuberculosis of the genital organs when a radical operation does not seem to be imminently necessary. It may also be employed where only a suspicion of tuberculosis exists.

Von Bungner's results are uncertain, because the method has only been employed for a short time, but it would appear to me that nevertheless a surgical operation should in the first place be undertaken, because the hopes of the instigator of the iodoform-injection method do not appear to me to be at all certain. Recently, however, a number of operators have appeared to give up the radical measures and adopted the milder ones, even going so far as to institute an expectant treatment. Some uphold that in most cases the epididymis is alone the seat of the disease, and that consequently destruction of the tuberculous foci seated within it is quite sufficient, and that castration is too radical, and should only be reserved for extreme cases. Senn claims good results by the sclerogenous method, but does not appear to be a strong advocate of its use.

Platon believes that the removal of one testicle in no way prevents the occurrence of the disease in the remaining organ, and should this arise it is hard to persuade a patient to lose his remaining seminal gland. Albert believes that he has also seen the disease appear in the remaining testicle and also the development of a general tuberculosis after castration has been done on one side, and for this reason he favors conservative treatment. Other authorities of late also oppose radical measures and deem that destruction of the diseased parts or ultimately an incision of the epididymis will be sufficient.

Among the conservative operations may be mentioned the experiments of Mauclaire, who endeavored to bring about atrophy of the testicle by ligation and section of the elements of the spermatic cord. It appeared to him that the best method was section of the entire spermatic cord, with the exception of the vas deferens and its accompanying vessels. Upon the appearance of the atrophic process, the tuberculous foci disappeared and a hard lump remained, which led the patient to believe that he still possessed his testicle.

It would appear to me, however, that the work done in this direction by Mauclaire has not been sufficiently controlled, and more recently there has been a tendency, not only to preserve the testicle itself, but also its functions as well, which, with the other methods described, were always lost.

Rasumowski, in an article which appeared in 1902, states that Bardenheuer tried to attain this end by endeavoring to give an exit to the semen by the formation of an anastomosis between the spermatic cord and the capsule of the testicle. To accomplish this the diseased epididymis was peeled out of its capsule and then the stump of the spermatic cord was sutured to the capsule, with the hope that the seminal fluid escaping from the rete testis would find its way into the space left by the excision of the epididymis and from there into the vas deferens, but this method naturally could never amount to anything. To form an anastomosis of any duration a simple mechanical union of the parts is not sufficient, for the reason that both mucosæ, covered with their epithelium, must be united in intimate relation to each other in the entire circumference of the anastomosis.

Rasumowski claims that he developed the same idea independently of Bardenheuer. He devised two methods of operation which would accomplish the same end; in one the indications for its use are when the entire epididymis has to be resected and a reunion of the vas deferens must be made with parts of the coni vasculosi. In the second operation the spermatic cord is united to the remainder of the epididymis when the tail and the part of the body of the latter have been removed. The technique of the first operation consists in resection of the epididymis, taking care that the vessels passing at the inner border of the epididymis to the testicle are carefully preserved. The cut end of the healthy part of the vas deferens is split up to the extent of about 1 cm., and, thus enlarged, it is stitched with fine catgut near to the rete testis, at a point where the epididymis was in close relation to the testicle. The sutures should only include the external connective tissue and muscular layers of the vas, while at the testicle the connective tissue of the corpus Highmorii is used. By this method the mucosa of both organs is supposed to be uninjured.

Now, in a certain sense, one is working in the substance of the testicle, and the connective tissue of the corpus Highmorii and that

of the albuginea should be securely sutured in a manner similar to that employed for the fixation of the drainage-tube in the wall of the stomach in Witzel's method of gastrostomy. These sutures are then buried by pulling over the remainder of the covering of the testicle and suturing them. A small drain is inserted and the scrotum closed.

In the second method of anastomosis of the vas and epididymis the diseased parts are first resected, the end of the vas is split, and then a canal is formed in the cut surface of the epididymis; this canal should be about 1 cm. deep. Fine catgut sutures are inserted in the external layers of the stump of the spermatic cord, both ends of the sutures being threaded on needles. The stump is then introduced into the canal, the sutures are drawn through to the surface of the epididymis, and are tied in such a manner that the spermatic cord is fixed into the substance of the epididymis. By this method the borders of the mucous layer come into close apposition with the coils of the cut epididymis, and in order to bring about a more perfect apposition the borders of the transverse section of the epididymis can be brought together around the inserted vas. The wound is then closed with drainage.

Should the case require the resection of a large amount of the spermatic cord, so that its insertion within the epididymis would cause considerable tension, or should the testicle be pulled upward too much in order to obtain approximation, the body of the epididymis should be separated from the testicle and by turning it upward the parts can be approximated. Rasumowski states that in cases where a portion of the testicle has already been removed on account of tuberculous infection, the last-mentioned technique can be employed by making anastomosis with the tubuli contorti and recti.

That by such means anastomosis can in reality be established is proven by experimental work, and Skaduto was able to demonstrate microscopically that the sexual gland could by this means preserve its functional relations; but whether or not this histological demonstration would be the same in man, and whether or not sexual activity can be continued without impediment, Rasumowski does not say. This modern method has been as yet insufficiently experimented with for any conclusion to be made, and, although it is most ingenious, I do not believe that practically it will ever be of any real value.

In opposition to those who believe in simple resection of the diseased parts and who are opponents to the radical treatment, there are other surgeons who believe that an operation cannot be too radical, because other parts of the urogenital apparatus are first involved, while the testicle is invaded by the tuberculous process only secondarily, consequently being involved in a descending extension. For this reason removal of the entire testicle is insufficient.

The tuberculous process continues to spread and the immediate good effect of the operation sooner or later proves to be an illusion.

In Germany a descending extension of urogenital tuberculosis is admitted by a large number of surgeons, and so eminent an authority as König believes that the testicle becomes involved by descending tuberculous process seated in the prostate or bladder, and that a primary infection of the seminal gland, without the disease being present in any other part of the body, is an exception. It was Gussenbauer's opinion that the testicle was involved secondarily by a descending infection of the disease. These authorities considered castration of one testicle as absurd, and they look upon double castration as practically useless, for the reason that if the affection involves one gland the disease already exists in the prostate and seminal vesicle. In their opinion another factor should also be taken into consideration, which would be decidedly against the entire removal of the testicle, namely, the mental effect of the operation. It has been shown by a number of writers that the internal secretions of the testicle play an important part in metabolism. These recent discoveries in physiology have worked riot among a number of surgeons, but we would consider attentively the ideas emitted by von Bruns, because of their importance and also for the light they throw upon the subject. In Kocher's writings, already mentioned, the idea is expressed that partial resection means only accomplishing half the necessary work, and it is also stated that the seminal gland is more involved than can clinically be detected, and that consequently recurrences are practically certain. Von Bruns emits the same opinion, and gives statistics showing that in 40 per cent. of his cases, six months after anything was noticed, the testicle was diseased, as proven at the time of operation. If the duration was over six months, it was present in 60 per cent. of the cases. Now, taking into consideration that the process often proceeds without any evident clinical changes, it can readily be conceived how little partial excision of the parts apparently involved can help the patient in the majority of cases, and how seldom a durable success can be recorded unless the entire seminal gland is removed.

Still another argument speaks against limited excision of the testicle, namely, that in about 50 per cent. of all cases of tuberculosis of the organ the disease at a later period develops in the other gland, and, according to the statistics of von Bruns, 23 per cent. of cases in which castration was performed on one side developed the disease in the remaining testicle. From this it may be concluded that prevention of the development of the disease in the apparently healthy testicle is to be found in early castration of the one afflicted. It stands to reason that the partisans of partial resection are baffled, and their various methods of interference have no significance whatever. The opponents of radical treatment declare castration superfluous, while others uphold that the operation is most disadvantageous to the patient, because the primary focus is left behind in the body. Of course, it is here understood that, according to their views,

tuberculosis of the testicle is due to a descending infection from the prostate and seminal vesicle, consequently a secondary process.

Baumgarten has thrown much light on this subject, for he has experimentally demonstrated on rabbits that tuberculosis of the bladder, in the pars prostatica urethræ, and in the prostate, could be produced by injecting cultures of very virulent tubercle bacilli, but he was never able to demonstrate tuberculosis of the spermatic cord or testicle. He observed the animals for a long period of time, and the process did not extend upward along the ureters. On the other hand, by experimentally infecting the testicle, he was able to demonstrate an ascending infection along the spermatic cord. In this case he injected the bacillus directly into the epididymis and the spermatic cord, and in order to avoid the objection that the virus might have attained the deeply seated part of the vas deferens he ligated it. It was also proven that none of the inoculation fluid entered the spermatic cord when injected into the epididymis, as no swelling of the cord near the epididymis could ever be found, and, microscopically, no tuberculous lesions could be demonstrated.

In all these experiments a rapid ascending extension of the process took place, but the testicle on the other side never became involved. Von Baumgarten rightly concludes, I believe, that the tuberculous process always follows either the current of secretions or the lymph, and never in an opposite direction. He believes that the explanation of this fact is to be found in the mode of living of the tubercle bacillus; this organism, being devoid of motion and being obliged to rely on passive transportation, must naturally follow the circulating currents. Beside this, they are unable to develop and grow in secretions, and for this reason they are powerless to resist the secretory currents unless retained by some obstruction.

Pathologically and clinically these experiments seem to be correct, and certainly coincide with facts, namely, that tuberculosis of the testicle often occurs when the other parts of the urogenital apparatus are intact. It would also go to show that descending infection by the bacillus of tuberculosis is impossible and that castration performed when the disease is still of short standing and not advanced will bring about a complete recovery, because it prevents the possibility of an ascending infection from taking place.

Von Bruns gives quite an imposing number of complete recoveries after castration of one testicle, namely, 46 per cent., and what makes it particularly valuable is that the observation of his cases continued over a period of thirty-four years.

If, however, one finds frequently other portions of the urogenital tract involved, it is only in very advanced stages of the process, especially where the prostate and bladder become infected secondarily from the testicle or by a descending infection from the kidneys. Only 12 per cent. died, according to von Bruns, from tuberculosis

of the urogenital apparatus after castration had been performed on one side, and in almost all of the fatal cases the patient presented the picture of tuberculosis of the urinary apparatus before the operation was undertaken. The same may be said regarding the cases of double castration, of which 15 per cent. died from tuberculosis of the urogenital apparatus, but the majority recovered, thanks to the operation. The ultimate duration of cure in double-sided castration amounted to 56 per cent., and the time over which the cases were observed was thirty years.

The great number of recoveries in which unilateral castration was done would seem to refute the statement that an extension of the process from one testicle to another takes place.

Equally favorable results have been reported by Simon, who, during the space of twenty-two years, had operated on 107 cases of tuberculosis of the testicle; the lapse of time during which they were followed varied from ten to twenty years. Out of 92 cases, 59 were alive, 54 of whom were free from any evidence of tuberculosis. Of the 33 who died, 26 succumbed to the tubercle bacillus and 7 from an intercurrent disease. 61 cases had remained free from tuberculosis after the operation, which gives us 66.3 per cent. recoveries. Simon learned the ultimate outcome in 29 out of 34 cases in which bilateral castration had been done, with the astonishing result that only 8 of them had died.

Regarding the question of psychical changes occurring after bilateral castration, it would appear to me that they have been considerably exaggerated, and where mental disturbances occur they usually only amount to a decrease in sexual desire.

The conclusions that may be deduced from what has been put forward in this paper, as well as from some little personal experience, would be that radical treatment should not be allowed to become obsolete, that castration has an exceedingly low mortality, considered as an operation, and that if performed at an early period of the disease there is a good chance of preventing further infection from the bacillus of tuberculosis from taking place. Castration certainly complies with one of the most urgent demands of modern therapeutics, namely, the eradication of the soil breeding the disease, when, of course, the affection has not been present for too long a period and has not extended to other parts of the body. Conservative surgery applied to the testicle is practically useless when the organ is affected by tuberculosis, and it allows the dangerous consequences to arise which the radical treatment directly tends to avoid.

THE RELATION OF CELLS WITH EOSINOPHILE GRANULATION TO BACTERIAL INFECTION.[1]

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In a preceding article I have described the behavior of the eosinophile cells during the course of experimental infection with a parasite belonging to the animal kingdom, namely, trichina spiralis. Both the polynuclear leukocytes with fine granulation and the coarsely granular eosinophile leukocytes of the blood are increased in number; but increase of eosinophlie cells constitutes the predominant feature of the local and hæmal leukocytosis which results. Infection with a large variety of bacteria, on the contrary, causes migration of finely granular leukocytes into tissues where bacteria or their products have accumulated, and, in addition, hæmal leukocytosis occurs. The behavior of the leukocytes with eosinophile granulation in the presence of bacterial infection, though repeatedly the subject of investigation, has not been clearly defined.

That the eosinophile cells have a part in resisting bacteria which have entered the body was first suggested by Hankin,[2] who maintained that the bactericidal substances of the blood serum are derived from the leukocytes with eosinophile granulation. Answering a critical review of this theory by Metschnikoff,[3] Hankin[4] subsequently stated that his observations made upon rabbits had reference to the amphophile or pseudoeosinophile cells of Ehrlich, and not to the coarsely granular cells which correspond to the eosinophile leukocytes of human blood.

Kanthack and Hardy,[5] following the suggestion of Hankin's hypothesis, studied in the frog the behavior of the eosinophile leukocytes in the presence of micro-organisms. If bacillus anthracis were injected below the skin of a frog, eosinophile cells, they found, accumulated in large numbers during the first three or four hours and collected in masses about the bacilli. Large cells with non-granular protoplasm and large nuclei, called by Kanthack and Hardy hyaline cells, then made their appearance, entered the masses of eosinophile cells, and finally ingested the bacteria. The micro-organism became the prey of the hyaline cell only after it had been

[1] The present investigation has been conducted with the aid of a grant from the Rockefeller Institute for Medical Research.

[2] Cent. f. Bakt., 1892, vol. xii. pp. 777, 809

[3] Ann. de l'Inst. Pasteur, 1893, vol. vii. p. 50.

[4] Cent. f. Bakt., 1893, vol. xiv. p. 852.

[5] Philosophical Transactions of the Royal Society of London, 1894, vol. clxxxv., B., part i. p. 279; and Proceedings of the Royal Society, 1894, vol. lii. p. 267.

subjected to the influence of eosinophile cells. Such influence, according to Kanthack and Hardy, is exerted by the granules of these cells. In hanging drops they saw the granules stream toward that side of the cell which happened to be in contact with the micro-organism and then gradually disappear.

Hardy and Wesbrook[1] have shown that when fresh cultures of the bacillus of anthrax or of the spirillum cholera are injected into the intestines of frogs, eosinophile cells migrate through the epithelium into the lumen, so that they finally disappear from the intestinal wall.

Mesnil,[2] studying the means by which lower vertebrates resist bacterial infection, has repeated many of the experiments of Kanthack and Hardy, but has not obtained the same results. Within two and a half hours after injection of bacillus anthracis into the dorsal lymph sac of the frog non-granular leukocytes with round or lobed nuclei begin to accumulate and immediately approach and ingest the bacteria. Leukocytes with eosinophile granulation may congregate at the point of inoculation, but their number is inconstant, and, while in some instances they constitute even 50 per cent. to 80 per cent. of the leukocytes at the site of inoculation, they are often, particularly in rana esculenta, not 1 per cent. of those present. That cells with eosinophile granulation in lower vertebrates do not play an essential part in resisting bacterial invasion is, Mesnil believes, further shown by the fact that the perch (perca fluviatilis), which is not susceptible to bacillus anthracis, possesses no granular leukocytes; injected anthrax bacilli, as in the frog, are engulfed by non-granular leukocytes possessing irregularly round or lobed nuclei. In accordance with the view held by Metschnikoff and himself, Mesnil believes that the eosinophile granules represent transformed material previously ingested by the leukocyte; such old phagocytes filled with reserve material still possess some remains of their phagocytic power. Mesnil states that he has observed these cells in the frog ingest bacteria, rarely after subcutaneous inoculation, but more frequently after the injection of bacteria into the circulation.

In a previous paper[3] I have reviewed the evidence which demonstrates, I believe, that the eosinophile cells of mammals are not derived from the polynuclear leukocytes with finer granulation, but exclusively from eosinophile cells in the bone-marrow. These cells of the marrow, which may be designated eosinophile myelocytes, are analogous to the myelocytes with finer granulation, the parent cells of the finely granular leukocytes. In lower vertebrates the relation of the various granular leukocytes to one another and to those of higher mammals are less clearly understood. In birds, for

[1] Journal of Physiology, 1895, vol. xviii. p. 490.
[2] Ann. de l'Inst. Pasteur, 1896, vol. ix. p. 301.
[3] The American Journal of the Medical Sciences, 1904, vol. cxxvii. p. 217.

example, the more common polynuclear leukocytes are provided with large spindle-shaped granules, which, like the less numerous coarsely granular leukocytes of mammals, have a strong affinity for eosin. Hence, conclusions reached by a study of lower vertebrates, some of which apparently possess no granular leukocytes, even were they in accord, are not with our present knowledge applicable to mammals.

In the article just mentioned I have considered certain facts which indicate that the polynuclear leukocytes with fine and with coarse granules in different mammalian species bear corresponding relations to one another. A second series of experiments performed by Kanthack and Hardy[1] on rabbits, guinea-pigs, and rats has, therefore, a more direct bearing upon the activities of the eosinophile cells in man and in other higher mammals. In mammals, as in lower vertebrates, according to Kanthack and Hardy, those wandering cells which are first attracted by micro-organisms and a variety of other irritant substances are coarsely granular oxyphile (eosinophile) cells, which have their origin in the neighboring connective tissue. This conclusion has been based upon a series of experiments in which various bacteria and a variety of substances, such as nitrate of silver, turpentine, and filtrates from bacterial cultures have been introduced into the peritoneal cavity or into the subcutaneous tissue of the animals just named.

If Ziegler's chambers containing cultures of bacillus anthracis or of the spirillum of cholera are introduced into the peritoneal cavity of the rabbit, at the end of seven hours only coarsely granular eosinophile cells have succeeded in entering. When a less virulent organism, such as bacillus ramosus, is employed, large non-granular cells with round or indented nuclei ("hyaline cells") have accumulated in large numbers at the end of two and a half hours. The more virulent bacteria, according to Kanthack and Hardy, cause rapid destruction of these non-granular cells, while the less virulent organism allows them to accumulate. In another series of experiments Kanthack and Hardy have injected bacillus anthracis, bacillus pyocyaneus, or the spirillum of cholera in small amount into the peritoneal cavity of the guinea-pig or of the rat. The primary result has been disappearance of the cells present in the cavity, and as fragments of eosinophile cells are to be found in the peritoneal fluid, they are believed to have been destroyed in part at least. The injected bacteria are quickly attacked by the coarsely granular cells, and even within five minutes after the inoculation of bacillus anthracis into the rat 40 per cent. of the eosinophile cells found are applied to bacilli. These cells do not ingest bacteria, but their granules, Kanthack and Hardy have maintained, exhibit the phenomenon noted in the frog. Bacteria are engulfed by the "hyaline" cells, the

[1] Journal of Physiology, 1894, vol. xvii. p. 81.

process beginning within ten minutes after inoculation. Destruction and removal of bacteria, they conclude, is due to the combined activity of two kinds of cells, the coarsely granular oxyphile (eosinophile) and the "hyaline" cell.

Durham[1] has studied the local reaction which occurs when various bacteria are injected into the peritoneal cavity of guinea-pigs. He has failed to observe the preliminary attack of eosinophile cells described by Kanthack and Hardy, and reaches the conclusion that these cells have no important part in the destruction of bacteria. Durham says, however, that in animals which die within thirty hours after inoculation, the only cells in the peritoneal fluid at the time of death are finely granular polynuclear leukocytes in abundance, together with a variable number of coarsely granular leukocytes. At times only one coarsely granular cell is seen in ten fields of the $\frac{1}{12}$ objective, while in other instances one may be found in almost every field. Judged by their relative numbers, the eosinophile cells at this stage, Durham believes, can have but a small share in the work of destroying bacteria.

Noesske[2] has performed experiments with the tubercle bacillus which have a bearing upon the present subject. Studying this organism under conditions which cause it to assume a radiate formation suggesting actinomycosis bovis, he found at an early stage of infection, about such colonies of the bacillus, free granules, which, he thought, were derived from eosinophile cells. He supported his views by demonstrating that the granules react to stains like eosinophile granules and are similarly affected by digestive ferments, but does not bring more conclusive evidence of their nature. Introduction of tubercle bacilli into the muscle of rabbits showed more clearly that eosinophile cells accumulate at the seat of infection. Colonies of bacillus tuberculosis were placed within an incision made into the muscle of the back, and at the end of four days the surrounding tissue was removed. In immediate contact with the implanted colonies the tissue was necrotic; polynuclear leukocytes were numerous, and eosinophile cells were few. Near-by, however, eosinophile leukocytes were present in great number within degenerate muscle fibres, among which were scattered tubercle bacilli. A similar result was produced in rabbits with tubercle bacilli killed with steam. Noesske, moreover, obtained an accumulation of eosinophile cells in the subcutaneous tissue of a human subject by injecting the dead bacilli. He reaches the conclusion that these cells are always abundant during the first stage of tuberculous infection. Pyogenic bacteria, on the contrary, Noesske found caused no accumulation of eosinophile cells.

Ehrlich[3] found that with acute leukocytosis only the mononuclear

[1] Journal of Pathology and Bacteriology, 1897, vol. iv. p. 338.
[2] Deutsche Zeitsch. f. Chirurgie, 1900, vol. lv. p. 211.
[3] Zeit. f. klin. Med., vol. i. part iii.

and neutrophile polynuclear forms of the blood are increased, while the eosinophile cells exhibit an apparent diminution. Subsequent observers have noted a well-marked diminution of the eosinophile leukocytes during various infectious diseases caused by bacteria. Müller and Rieder[1] have found that eosinophile cells are diminished during typhoid fever. Rieder[2] noted their diminution or complete absence from the blood in cases of pneumonia, while Canon[3] noted a diminution in association with septic processes. Zappert[4] has carefully studied the behavior of the eosinophile leukocytes during the course of various infectious diseases, and reaches the conclusion that fever is associated with such constant diminution of the absolute number of these cells that this diminution may be regarded as one of the manifestations of febrile intoxication. With pneumonia, typhoid fever. erysipelas, and certain pyogenic infections eosinophile cells are diminished so long as fever persists, but after its subsidence return to normal or, in a certain proportion of cases, undergo a more or less well-marked increase above their normal number. Zappert quotes observations of Ehrlich[5] upon the destruction of leukocytes in the spleen during febrile processes, and reaches the conclusion that eosinophile cells are diminished because the normal transformation of leukocytes with neutrophile granulation into eosinophile leukocytes is prevented.

Observations similar to those of Zappert have been made by Türk[6] and others in cases of pneumonia, typhoid fever, diphtheria, and with various suppurative processes. It is, however, noteworthy that in certain diseases not due to bacterial infection, such as scarlet fever (Kotschetkoff[7]) and smallpox (Ferguson[8]), there is a moderate increase of eosinophile cells.

In hardened tissues which have been the seat of a variety of inflammatory procesess several observers have noted the presence of eosinophile cells, occasionally in considerable number. Numerous observations have shown that eosinophile cells are often abundant in carcinomata of the cervix uteri, in nasal polyps, and in a variety of other benign and malignant tumors. From a study of tissue obtained at autopsy and from the operating table, Noesske[9] reached the conclusion that tumors of mucous membranes, particularly when they are exposed to injury, are rich in eosinophile cells; immense numbers are not infrequently found in epitheliomata of the lip or of the tongue, in carcinomata of the cervix uteri, and in laryngeal

[1] Deutsches Arch. f. klin. Med., 1891, vol. xlviii. p. 47.
[2] Beiträge zur Kenntniss der Leukocytoses, Leipzig, 1892.
[3] Deutsche med. Woch., 1892, vol. xviii. p. 206.
[4] Zeit. f. klin. Med., 1893, vol. xxiii. p. 227.
[5] Zur Kenntniss des acuten Milztumors, Charité-Ann., 9 Jahr.
[6] Klinische Untersuchungen über das Verhalten des Blutes bei Infectionskrankheiten, Wien und Leipzig, 1898.
[7] Ref., Cent. f. allg. Path. u. path. Anat., 1892, No. 11.
[8] Journal of Pathology and Bacteriology, 1908, vol. viii. p. 411.
[9] Loc. cit.

tumors. Tumors situated below the skin contain eosinophile cells when the overlying epithelium is lost and ulceration is beginning. When benign or malignant tumors are situated in internal organs where they are protected from infection, eosinophile cells are scant or absent. Noesske thinks that these cells have a part in protecting the tissue from bacterial infection. Where, however, the tumor tissue is the seat of an advanced inflammation, and, indeed, in the lesions of various pyogenic or other inflammatory processes, such as erysipelas, osteomyelitis, and pneumonia, eosinophile cells are present in small number or are completely absent. Eosinophile cells, at times in very large number, have been found by Howard and Perkins[1] in the lesion of appendicitis, salpingitis, oöphoritis, and perioöphoritis, acute interstitial and suppurative nephritis, enteritis, and of a variety of other inflammatory processes. Their association with such lesions has not been found constant, and in some instances they are normally present in the affected tissue.

In an article to which reference has already been made, I have collected evidence to show that the bone-marrow is the seat of origin of the eosinophile leukocytes, and the vascular system the path by which they are distributed to various tissues of the body. Changes in the blood being subject to observation during the entire course of an experimental infection, it is possible to determine if the eosinophile cells of the blood exhibit a characteristic reaction to bacterial invasion.

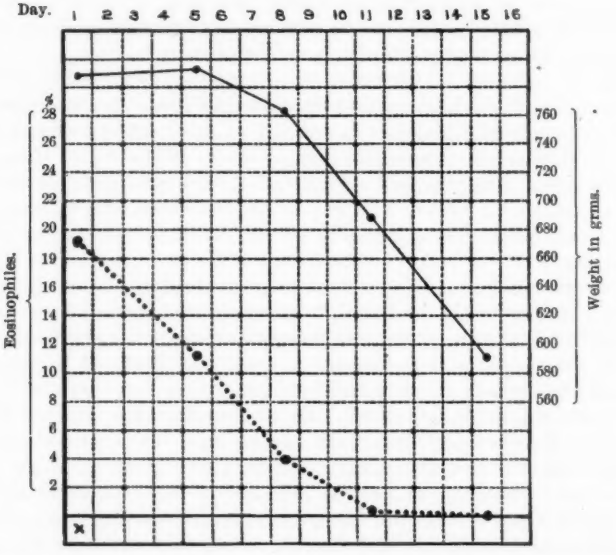
METHODS. In counting the relative and absolute number of eosinophile leukocytes in the blood, I have used the methods previously described.[2] For the purpose of these experiments the guinea-pig has been found particularly suitable, since the blood of apparently healthy full-grown animals usually contains from 5 per cent. to 10 per cent. of eosinophile leukocytes. Hence the effect of conditions which cause a diminution of these cells can be far more accurately determined than in animals possessing only a very small proportion of such cells. In order to test the behavior of the eosinophile cells, I have employed a variety of bacteria, including bacillus tuberculosis, bacillus anthracis, bacillus choleræ suis, and bacillus mucosus capsulatus (of Friedländer), all of which are pathogenic in small quantity for guinea-pigs. Bacillus pyocyaneus has been selected as a convenient means of studying the effect of a relatively severe infection from which the animal is capable of recovering. Bouillon cultures incubated from twenty-four to forty-eight hours have been employed in varying amount. The injection of as much as 3 c.c. of sterile bouillon into the peritoneal cavity has caused no noteworthy change in the number of eosinophile cells nor in the weight of the animal.

[1] Johns Hopkins Hospital Reports, 1902, vol. x. p. 249.
[2] Loc. cit.

Behavior of the Eosinophile Leukocytes during the Course of Fatal Bacterial Infection.

Infection of guinea-pigs with a moderate number of trichinæ, I have shown,[1] causes a gradual increase of the eosinophile leukocytes, but death is preceded by rapid diminution. The administration of a very large number of parasites is more quickly fatal; the eosinophile cells diminish in number and completely disappear from the blood. The effect of fatal bacterial infection is similar, though the eosinophile cells may disappear from the circulating blood more gradually.

CHART I.



Showing changes in the percentage of eosinophile leukocytes (dotted line), and in weight (straight black line), caused by infection with bacillus tuberculosis. The day of inoculation in this and in subsequent charts is marked by a ×.

Chart I. records the proportion of eosinophile leukocytes in the blood and the weight of a large guinea-pig which received into the subcutaneous tissue of the abdominal wall 0.5 c.c. of a suspension in bouillon of bacillus tuberculosis. Two days before death eosinophile cells had almost completely disappeared from the blood.

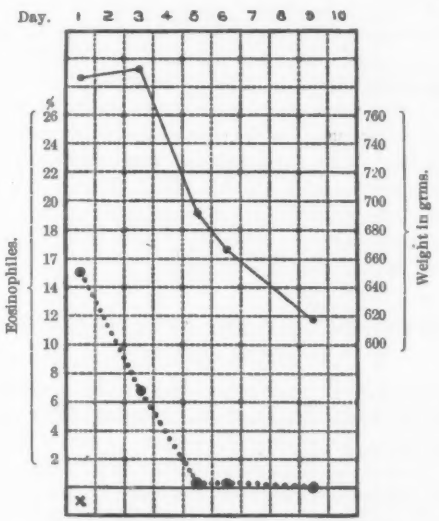
Chart II. records the percentage of eosinophiles and the weight of a large animal which received subcutaneously 0.5 c.c. of a bouillon

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, March, 1904.

culture of bacillus choleræ suis incubated twenty-four hours. Death did not occur until the ninth day, but the eosinophile leukocytes, which at the beginning of the experiment constituted 15 per cent. of the white blood corpuscles, had almost completely disappeared on the fifth day.

In both experiments the tissues from the animals were hardened in Zenker's fluid and stained, after embedding in paraffin, with hæmatoxylin and eosin, so that eosinophile cells might be identified. The paucity of eosinophile cells in the tissues in both experiments is in harmony with their disappearance from the blood. In the spleen, where the number of eosinophile cells normally present corresponds

CHART II.



Showing changes in the percentage of eosinophile leukocytes (dotted line) and in weight (straight line), caused by infection with bacillus choleræ suis.

approximately to their number in the circulating blood, no eosinophile cells are found. In the mucosa of the small intestine, even in the neighborhood of Peyer's patches, none have been found in the sections examined. In a mesenteric lymphatic gland from the animal injected with the bacillus of hog cholera only a few scattered eosinophile cells are found. Particularly remarkable is the small number of cells with eosinophile granulation present in the bone-marrow; myelocytes occur, but are sparsely scattered, while the almost complete absence of smaller eosinophile cells with lobed nuclei is noteworthy. In the bone-marrow from both animals occur

very small eosinophile cells, with a diameter approximately two-thirds that of an eosinophile leukocyte. These dwarfed cells have nuclei which are round or only slightly indented, resembling in the latter case intermediate stages between the nucleus of the myelocyte and the typically lobed nucleus of the mature eosinophile leukocyte.

With bacterial infections which are more acute than those just described, eosinophile leukocytes disappear much more quickly from the circulating blood; indeed, none may be found in specimens examined at the end of a few hours. Injection of 1 c.c. of a bouillon culture of bacillus pyocyaneus, which had been incubated four days, into the peritoneal cavity of a guinea-pig possessing 5.7 per cent. of eosinophile leukocytes, caused their disappearance within twenty-four hours; death occurred at the end of forty hours. Subcutaneous inoculation of 0.5 c.c. of a twenty-hour culture of the same organism caused the percentage of eosinophile leukocytes to fall from 9.7 to 0.5 in eight hours. Bacillus mucosus capsulatus (0.3 c.c. of a forty-eight-hour-old bouillon culture injected into the peritoneal cavity) caused the eosinophile leukocytes to diminish during four hours from 20.7 per cent. to 7.3 per cent. of the number of white blood corpuscles. The injection of streptococcus pyogenes into the peritoneal cavity had a similar effect; 1 c.c. of a culture four days old caused the eosinophiles of a guinea-pig possessing 5.7 per cent. to diminish to such an extent that none were found in a specimen examined at the end of four hours.

Behavior of Eosinophile Leukocytes during the Course of Non-fatal Bacterial Infection.

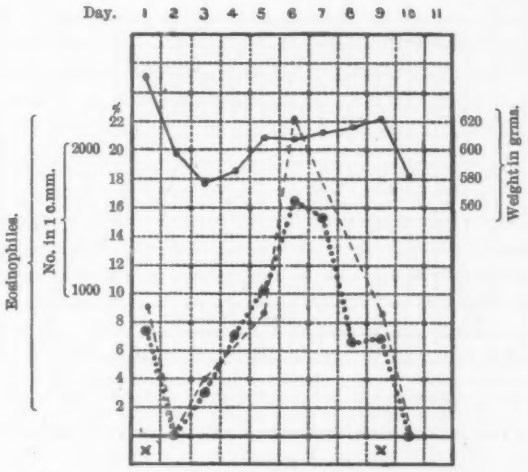
The disappearance of eosinophile leukocytes under the influence of severe, usually fatal infections has suggested the desirability of studying their behavior during the course of acute infections from which the animal is capable of recovery. For this purpose bacillus pyocyaneus has been selected and has been injected into the peritoneal cavity in order to avoid the prolonged effect of a localized abscess. The injection of 0.5 c.c. to 1 c.c. of a culture in bouillon incubated at 37° C. during twenty-four hours causes an acute general peritonitis, from which the animal usually recovers. The well-known effect of such inoculation upon the blood being an increase of the polynuclear leukocytes with fine granulation, I have limited my attention to the behavior of the eosinophile cells.

Chart III. records the effect of the intraperitoneal inoculation of 0.7 c.c. of a bouillon culture of bacillus pyocyaneus upon a large guinea-pig of which the eosinophile leukocytes constituted 7.3 per cent. of the white corpuscles.

At the end of twenty-four hours after inoculation eosinophile leukocytes had diminished to such extent that none were found in the specimens of blood examined. The proportion gradually rose

and reached a maximum on the sixth day, when it exceeded that originally present; on the eighth day the percentage count agreed approximately with that before inoculation. The absolute number of eosinophile cells has been estimated from the total number of leukocytes, counted daily by the same Thoma-Zeiss apparatus, and the changes which it undergoes are found to correspond with those of the percentage count. The weight of the animal has been recorded, since it gives an indication of the effect of infection upon the general metabolism of the animal.

CHART III.



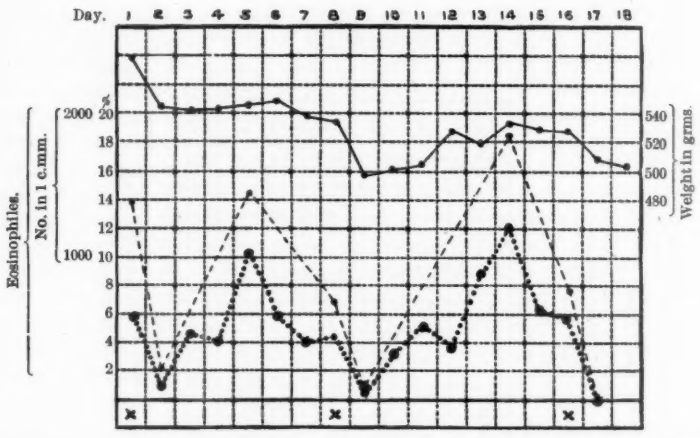
Showing changes in the percentage (dotted line) and in the absolute number (broken line) of eosinophile leukocytes after infection with bacillus pyocyaneus. On the first day 0.7 c.c. of a bouillon culture twenty-four hours old was injected, and on the ninth day this dose was repeated. The animal was killed on the tenth day. The weight is indicated by an unbroken straight line.

Chart IV. is appended in order to confirm the results just described. The small dose (0.5 c.c.) of bacillus pyocyaneus injected on the first day was followed by a much less marked increase of eosinophiles than that consequent upon the second larger dose (1 c.c.). In these experiments, as in that recorded by Chart III., decrease of eosinophile cells to almost complete disappearance is the first effect of inoculation; a somewhat gradual increase follows and reaches a maximum on the fifth or sixth day, when, after inoculating 0.7 c.c. or 1 c.c. of the culture, the number of eosinophile cells in 1 c.mm. of blood is more than twice the original number. A return to normal then follows. Such changes in the blood suggest that destruction of eosinophile cells has been followed by regenera-

tion causing an accumulation in excess of the normal. In order to obtain an explanation of this phenomenon it is essential to know the cause of their temporary disappearance during what may be termed the stage of eosinophile leucopenia.

In order to determine the fate of the eosinophile leukocytes which have disappeared from the peripheral circulation during the early stages of acute bacterial infection attention has been directed

CHART IV.



Showing the effect of infection with bacillus pyocyaneus. On the first day 0.5 c.c., on the eighth day 1 c.c. of a culture twenty-four hours old was injected; on the sixteenth day the animal received 1 c.c. of a culture four days old, and death occurred on the eighteenth day.

to the seat of infection. For the study of the local changes which follow inoculation the peritoneal cavity offers obvious advantages. The inflammatory exudates which accumulate can be readily obtained while the phenomena occurring in the tissues can be conveniently studied in preparations made from the transparent tissue of the omentum and mesentery.

Local Accumulation of Eosinophile Leukocytes after Intraperitoneal Inoculation of Bacteria.

Since previous studies have shown that local accumulation of eosinophile cells is the result of their migration from the blood-vessels, it has been considered desirable to study with especial care the contents of the vessels at the site of inoculation and to note perhaps the occurrence of migration. For this purpose the following method has been employed: At the end of a variable time after inoculation the animal is etherized and, while breathing still con-

tinues, the peritoneal cavity is opened in the midline. After specimens of the peritoneal exudate have been prepared, Zenker's fluid (containing 5 per cent. of acetic acid) warmed to a temperature of 40° C. is poured into the cavity. The omentum and mesentery, together with the peritoneum elsewhere, are thus quickly hardened. The tissues to be preserved are removed and kept in Zenker's fluid about twenty-four hours, after which they are treated in the usual way. Small pieces of the omentum and mesentery are stained without embedding. Treatment of these membranes, previously stained with hæmatoxylin, with 0.5 per cent. aqueous solution of eosin has served to demonstrate so clearly the granules of the eosinophile leukocytes that these cells are readily distinguishable from the more numerous polymorphonuclear leukocytes with fine granulation; at the same time they are recognizable within the blood-vessels. The amœboid shape of the leukocytes is often well preserved and not infrequently they are fixed in process of migration from the vessels. Methylene blue used with eosin has the advantage of staining bacteria.

The peritoneal cavity contains normally a small amount of clear fluid in which are suspended a considerable number of cells. The character of these wandering cells has been the subject of special study by Kanthack and Hardy, who found the following varieties: 1. Polymorphonuclear cells with coarse eosinophile granules forming in guinea-pigs from 30 per cent. to 50 per cent. of the total number of cells. 2. Cells with basophile granulation occurring in small number. 3. Small cells, identical with the lymphocytes of the blood, possessing a single round nucleus surrounded by a narrow rim of protoplasm. 4. Larger mononuclear cells with round or indented nuclei and fairly abundant non-granular protoplasm. The latter Kanthack and Hardy designate "hyaline cells." Both Durham and Beattie have found in the peritoneal cavity of guinea-pigs three types of wandering cells described by Kanthack and Hardy, but have not noted the presence of cells with basophile granulation. The "hyaline cells" of these authors in part at least are the macrophages of Metschnikoff.

Before describing my observations upon the behavior of the eosinophile cells in the presence of bacterial infection I will briefly define the reaction which occurs when bacteria are injected into the peritoneal cavity. These changes have been studied by Issaeff,[1] Metschnikoff,[2] Durham,[3] and Beattie.[4] The first effect of intraperitoneal inoculation is the partial disappearance of cellular elements normally present, so that in the guinea-pig, according to Durham, five or six minutes after injection almost all cells save lymphocytes have disappeared.

[1] Zeit. f. Hygiene, 1894, vol. xvi. p. 287. [2] Ann. de l'Inst. Pasteur, 1895, vol. ix. p. 369.
[3] Journal of Pathology and Bacteriology, 1896, vol. iv. p. 338.
[4] Ibid., 1903, vol. viii. p. 129.

This stage of leucopenia persists about one hour (Durham), during which time the amount of peritoneal fluid increases. Metschnikoff has maintained that the disappearance of leukocytes is the result of their destruction by the toxic products introduced with the micro-organisms. Durham has brought forward evidence to support a different explanation. At the end of only two minutes after injection he has noted that "hyaline" and eosinophile cells begin to adhere in clumps, the lymphocytes being exempt. At first these groups are small, but later large masses containing many cells may be found. Such masses tend to adhere to the peritoneal surfaces, but especially to the omentum, so that at the end of about twenty minutes (Durham) "hyaline" and eosinophile cells are here present in considerable number. At the end of about an hour polynuclear leukocytes with fine granulation make their appearance and subsequently accumulate so that about fifteen hours after inoculation they are present in enormous number. They are actively phagocytic and ingest bacteria. If, however, infection is caused by a large dose of a virulent organism, few polynuclear leukocytes may be found and the stage of leucopenia may persist until death. With a relatively mild infection which has caused the accumulation of polynuclear cells in great number, cells of another type appear at the end of about fifteen hours. They are larger than polynuclear leukocytes and have a large round, oval, or indented nucleus. These cells, which are the macrophages of Metschnikoff, are actively phagocytic and ingest not only bacteria but polynuclear leukocytes as well, so that frequently several of the latter are seen within one macrophage. Upon the fourth, fifth, or sixth day after infection, the peritoneal fluid has assumed its normal characters, disappearance of the polynuclear leukocytes being followed by that of the macrophages.

Observers who have studied the foregoing phenomena have not failed to note the presence of eosinophile cells in the exudate which accumulates. Such cells, however, exist in the normal peritoneal cavity, and the difficulty of determining whether they are increased or diminished is considerable. The divergent conclusions reached by observers who have studied the effect of intraperitoneal inoculation have already been cited.

Study of the blood has shown that eosinophile cells partially or completely disappear from the peripheral circulation within a few hours after intraperitoneal inoculation. Study of the membranes which are contained within the peritoneal cavity has explained this phenomenon. Eosinophile cells constitute a considerable proportion of the immense number of leukocytes which within several hours are attracted to the bloodvessels which abut upon the infected peritoneal surface. Their migration and accumulation within the peritoneal cavity are demonstrable. These facts may be best illustrated by a series of experiments performed with *bacillus pyo-*

cyaneus. The following observations have been made upon fourteen animals inoculated intraperitoneally and killed after intervals varying from a few minutes to twenty-four hours:

Within a few minutes after the injection of one cubic centimetre of a bouillon culture of bacillus pyocyaneus incubated twenty-four hours large mononuclear and eosinophile cells disappear from the peritoneal cavity, so that in animals killed at the end of eight and fifteen minutes after inoculation only one or two eosinophile leukocytes have been encountered while counting several hundred cells, almost exclusively lymphocytes. Examination of the omentum fixed and stained confirms the statements of Durham. Large mononuclear cells form compact clumps, often containing a hundred or more cells, among which are eosinophile cells in varying number. Altered or fragmented eosinophile cells were not seen, and evidence that these cells had undergone destruction was not obtained. In animals killed at the end of eight, fifteen, or thirty minutes after inoculation the number of leukocytes within the bloodvessels of the omentum and mesentery has undergone no change. Within small veins having a diameter equal or twice that of a polynuclear leukocyte, white corpuscles are scattered among the red corpuscles at such long intervals that the labor of counting them is considerable. In the tissue of the mesentery eosinophile cells occur in considerable number, but are not more numerous than in the normal animal.

At the end of one hour the number of cells in the peritoneal exudate is still small, though polynuclear leukocytes with fine granulation have made their appearance. Eosinophile cells are also present in small number. In the tissue of the mesentery a few polynuclear leukocytes are found about many of the bloodvessels. Within the lumen of the vessels leukocytes are much more numerous than before and are in large part finely granular polynuclear leukocytes, some of which are flattened out upon the endothelial surface of the vessel, while others are in process of migration.

At the end of two hours the same changes are more advanced. In the peritoneal exudate cells are not numerous and about one-half of those present are polynuclear forms with fine granulation; eosinophile cells are fairly numerous and constitute about 10 per cent. Leukocytes have accumulated in the bloodvessels of the mesentery and are often found in fair number about them, while cells in process of migration are numerous. Eosinophile cells are present both in the tissue and within the bloodvessels, but their proportion does not differ notably from that in the peripheral circulation before inoculation. In an animal (weight 553 grams), of which the eosinophile leukocytes numbered 5.7 per cent. before inoculation, 4 per cent. were counted in small veins in diameter about twice that of a polynuclear leukocyte. Since, however, the total number of leukocytes within these vessels has been enormously increased,

such percentage indicates that many eosinophile cells have been held in the vessels of the inflamed region. Eosinophile cells are occasionally found in process of migration.

At the end of four hours the influence of bacterial infection upon the eosinophile leukocytes is more clearly demonstrable. The omentum is now covered by purulent exudate and, as Durham has described it, is rolled into a compact mass lying in contact with the stomach. In the peritoneal cavity is a considerable amount of turbid fluid containing an immense number of cells which are almost wholly polynuclear leukocytes. Eosinophile cells are present, but in small number, so that one or two are encountered while counting successive hundreds of cells. In the tissue of the mesentery polynuclear leukocytes are numerous and eosinophile cells are present in smaller proportion. In the bloodvessels leukocytes are closely crowded and eosinophile cells are very numerous. In blood from the ear of a guinea-pig weighing 604 grams the eosinophile leukocytes which had constituted 8.3 per cent. of the white corpuscles before inoculation had fallen at the end of four hours to 1.3 per cent. The animal was killed within the next half-hour. In small veins of the mesentery with a diameter from three to four times that of a polynuclear leukocyte, 21, 26, 20, and 23 eosinophile leukocytes were counted in successive hundreds of white corpuscles, which are here present in very large numbers. In smaller vessels with a diameter approximately half as great, leukocytes are less numerous and a smaller number of eosinophile cells are present, the count in two successive hundreds being 11 and 13. Where eosinophile cells are so numerous the process of migration is readily demonstrable. Some cells with eosinophile granulation are flattened and closely applied to the inner surface of the vessel; others have been fixed while making their way through the wall of the vessel, part of the cell being still within the lumen, while a part has penetrated the intima and projects upon the outer surface of the small vein which is formed by little more than a layer of endothelial cells. That part of the leukocyte which projects from the vessel wall is occasionally connected with the remainder, still in the lumen of the vessel, by a strand of protoplasm drawn out into a narrow thread. Upon the surface of the omentum polynuclear leukocytes are present in great number and are usually collected to form compact clumps. Within and about such masses eosinophile leukocytes are numerous. In the bloodvessels of the omentum, polynuclear leukocytes, both with fine and with coarse granulation, are abundant.

At the end of eight hours polynuclear leukocytes are present in the peritoneal exudate in immense number and are in large part collected into masses held together by a network of fibrin. From 1 to 2 per cent. of eosinophile cells can be counted in the fresh exudate. The masses of leukocytes just mentioned are particularly numerous upon the surface of the retracted omentum. In

specimens of the omentum stained with eosin and methylene blue eosinophile cells are clearly demonstrable even though embedded in masses of finely granular leukocytes, and are particularly numerous within the clumps of leukocytes already mentioned. From such specimens one obtains convincing evidence that eosinophile cells in number far greater than that originally present have found their way into the peritoneal cavity.

Eosinophile leukocytes upon the surface of the omentum are in part normal in appearance and are provided with lobed nuclei which stain most deeply at the periphery. Eosinophile cells exhibiting degenerative changes are however, readily found. Though the eosinophile granules are still well preserved, the nucleus of the cell is contracted into one or more small round masses which stain deeply and homogeneously. While the finely granular leukocytes almost uniformly contain many ingested bacteria, the bodies of the eosinophile cells are free from such inclusions.

Examination of the mesentery demonstrates that leukocytes are less numerous in the small bloodvessels than at an earlier period. Though polynuclear leukocytes and eosinophile cells are still abundant, migration is less active and at the end of sixteen hours has apparently ceased completely.

At the end of sixteen hours eosinophile leukocytes still form a conspicuous feature of the exudate upon the surface of the omentum and to less extent upon the surface of the mesentery. Many are still well preserved, but a considerable proportion exhibit degenerative changes, the nucleus being contracted into one or more small masses of chromatin which stain deeply and homogeneously. Occasionally a clear vacuole is situated within the otherwise compact globule of chromatin. In some instances, on the contrary, the lobed nucleus of the eosinophile cell is swollen and stains poorly. Changes of a similar nature affect the nuclei of the finely granular polynuclear leukocytes. At this stage large mononuclear cells have made their appearance.

At the end of twenty-four hours large mononuclear cells have become numerous. Eosinophile leukocytes form a small proportion of the great number of cells present in the exudate. Ingestion of polynuclear cells by the large mononuclear phagocytes has begun. In this process the eosinophile and finely granular leukocytes are equally concerned, and within a macrophage may be found a round clump of coarse eosinophile granules from which the nucleus has completely disappeared.

In order to confirm the preceding observations, repeating the experiments, I have employed, instead of bacillus pyocyaneus, bacillus mucosus capsulatus (of Friedländer), an organism far more pathogenic for guinea-pigs.

Experiment A (*Bacillus Mucosus Capsulatus*). An animal weighing 492 grams received 0.3 c.c. of a bouillon culture twenty-

four hours old. The eosinophile leukocytes before inoculation constituted 3.3 per cent. of the white blood corpuscles. In the peritoneal exudate at the end of three hours free bacteria are present in large number; polynuclear leukocytes, lymphocytes, and eosinophile cells are present, the latter forming 35.3 per cent. In the tissue of the mesentery leukocytes occur in moderate number. In the small veins leukocytes are very numerous, and in four successive hundreds of white corpuscles the proportion of eosinophile leukocytes was 14, 17, 13, and 17 per cent. Eosinophile cells are found fixed in process of migration.

Experiment B (*Bacillus Mucosus Capsulatus*). An animal weighing 625 grams received intraperitoneally 0.3 c.c. of a culture of bacillus mucosus capsulatus forty-eight hours old. The eosinophile leukocytes in the peripheral circulation which before inoculation numbered 24.3 per cent. fell at the end of four hours to 7.3 per cent. The animal was killed at the end of four and a half hours. Cells are fairly numerous in the peritoneal exudate and are almost wholly polymorphonuclear leukocytes and eosinophile cells, the latter constituting 7.7 per cent. In the mesentery polynuclear leukocytes and eosinophile cells occur in considerable number, particularly in the neighborhood of the bloodvessels. In the vessels leukocytes are usually accumulated in such number that the lumen is closely packed with cells of which eosinophile leukocytes constitute considerably more than half. To obtain an approximate estimation of their relative number they were counted in small vessels with a diameter from one and a half to twice that of an eosinophile cell; the percentage count was 65 per cent. Many of these cells are found flattened and closely applied to the endothelial surface of the vessel, while others are found in process of migration; a small process containing part of the nucleus may project between the endothelial cells, the remainder of the leukocytes being within the lumen. Sections of the mesentery embedded in paraffin confirmed the observations just described. In the lumen of one comparatively small vein differential count showed the presence of 73 per cent. of eosinophile leukocytes.

Experiment C (*Bacillus Mucosus Capsulatus*). A guinea-pig weighing 597 grams, with eosinophile leukocytes numbering 20.3 per cent., received intraperitoneally 0.5 c.c. of a bouillon culture of bacillus mucosus capsulatus. The animal died at the end of twenty hours, and the peritoneal cavity was found to contain about 3 c.c. of turbid fluid in which polynuclear leukocytes numbered 69 per cent., eosinophile cells 29 per cent., and large mononuclear cells 2 per cent.

The phenomena which occur after inoculation with bacillus pyocyaneus are reproduced by infection with bacillus mucosus capsulatus. The experiments with the two organisms are not wholly comparable, since the number of eosinophile leukocytes in the

circulating blood before inoculation in different animals has differed considerably. Nevertheless, with the more virulent bacillus mucosus capsulatus migration of eosinophile cells appears to be much more active, so that at the end of a given time the proportion of eosinophile leukocytes in the peritoneal exudate is much greater than with bacillus pyocyaneus. The chemotactic influence which virulent bacteria exert upon the eosinophile cells is further shown by study of the bloodvessels in the mesentery. In two of the experiments just described eosinophile leukocytes constituted respectively 65 per cent. and 15.2 per cent. of the total number of white corpuscles in these vessels, though their proportion in the peripheral circulation before inoculation had been only 24.3 per cent. and 3.3 per cent. Doubtless the earlier migration of polynuclear leukocytes with fine granulation explains in part the large proportion of eosinophile leukocytes present in the vessels three or four hours after inoculation. The experiments demonstrate that both types of polymorphonuclear leukocyte are attracted to the inflamed region.

Results of a similar nature have been obtained with *bacillus anthracis*.

Experiment A (*Bacillus Anthracis*). A guinea-pig weighing 533 grams, with eosinophile leukocytes numbering 27.3 per cent., received into the peritoneal cavity 0.5 c.c. of a bouillon culture of bacillus anthracis forty-eight hours old. At the end of four hours the animal was killed. The peritoneal exudate is found to contain polynuclear leukocytes in great number, together with eosinophiles, constituting 7 per cent. of the cells present. In the tissue of the mesentery eosinophile cells are numerous. The small bloodvessels are closely packed with leukocytes, among which those with eosinophile granulation, counted in small veins with a diameter approximately one and one-half that of a leukocyte, constitute in three successive hundreds 23, 21, and 20 per cent.

In the foregoing experiment it is evident that a large number of eosinophile leukocytes have been held in the inflamed area, even though it be recalled that their proportion in the peripheral circulation before inoculation slightly exceeded that found in the vessels of the mesentery four hours later, for they then constituted one-fifth of the immense number of leukocytes which are crowded together in the vessels of the inflamed membrane. With bacillus anthracis, as with bacillus pyocyaneus (see Chart IV.), a small dose of the micro-organism has a less marked influence upon the eosinophile cells.

Experiment B (*Bacillus Anthracis*). A guinea-pig weighing 560 grams, with eosinophile leukocytes in the peripheral circulation numbering 2.3 per cent., was inoculated with 0.1 c.c. of a twenty-four-hour-old culture of bacillus anthracis. At the end of four hours the peritoneal exudate contained polynuclear leukocytes in great number, together with eosinophiles, constituting 2.2 per cent. of the cells

present. Of the leukocytes which are closely packed together in the bloodvessels of the mesentery 1 per cent. are cells with eosinophile granulation.

Accumulation of Eosinophile Myelocytes in the Spleen.

Study of the spleen during the first few hours which follow bacterial inoculation of the peritoneal cavity has afforded further evidence of a profound disturbance of the eosinophile cells. In the venous sinuses of the spleen four hours after inoculation are found both finely granular and coarsely granular or eosinophile myelocytes, together with a small number of giant cells identical in structure with the so-called megakaryocytes of the bone-marrow.

When a rabbit is repeatedly bled the spleen undergoes what has been designated by Dominici[1] "myeloid transformation." Cells which are characteristic of the bone-marrow make their appearance in the organ. During the course of prolonged infection with the bacillus of typhoid fever, Dominici has observed a similar phenomenon, but all the cells peculiar to the marrow are not represented, megakaryocytes and eosinophile cells being rare or absent. In the spleen of three guinea-pigs killed eighteen weeks after inoculation with bacillus tuberculosis, Dominici[2] found myelocytes both with fine and with coarse (eosinophile) granulation and megakaryocytes. Dominici believes that new formation of myeloid tissue occurs in the spleen, so that the organ again takes on the hæmatopoietic activity which it normally possesses only during embryonic life.

Muir, moreover, has found myelocytes in the spleen of rabbits subjected to repeated infection with staphylococcus pyogenes aureus. He has not attempted to distinguish forms with fine and coarse granulation. He has observed similar cells in the circulating blood and thinks that it is a function of the spleen to remove such abnormal elements from the blood.

In the spleen of individuals dead with scarlet fever, diphtheria, erysipelas, septicæmia, pneumonia, peritonitis, purulent meningitis, and phthisis Hirschfeld[3] has found both neutrophile and eosinophile myelocytes. Since, he says, myelocytes have been found (Engel,[4] Türk[5]) in the blood in association with the hyperleukocytosis of infectious diseases, it may be suspected that those in the spleen are derived from the bone-marrow. Against this view is the occurrence in the spleen of eosinophile myelocytes which have never been observed in the blood with hyperleukocytosis. Hirschfeld maintains that he has found transitions between the non-granular

[1] Arch. de médecine expérimentale, 1901, vol. xiii. p. 1.
[2] Compt. rend. Soc. de biol., 1900, p. 851.
[3] Berliner klin. Woch., 1902, vol. xxxix. p. 701.
[4] Deutsche med. Woch., 1897, Nos. 8 and 9.
[5] Loc. cit.

lymphoid elements of the spleen and the granular myelocytes, which can thus, he thinks, be formed within the organ.

I have observed the occurrence of eosinophile myelocytes in the spleen after inoculation with bacillus pyocyaneus, bacillus anthracis, and bacillus mucosus capsulatus. For control the spleens from six apparently healthy guinea-pigs have been carefully studied. Eosinophile leukocytes in the circulating blood of these animals just before death varied in different animals from 0.3 to 17.2 per cent. Eosinophile cells which are identical with those of the blood are readily recognizable, both in the sinuses of the spleen and in the intervening pulp, and are particularly numerous when the proportion of eosinophile leukocytes in the blood has been large. Eosinophile myelocytes have not been found. The spleens from two animals which had been killed respectively during the third and fourth week after infection with trichina spiralis were also examined. In one instance the proportion of eosinophile leukocytes in the peripheral circulation had increased from 5.7 to 17.3 per cent., in the other from 6.7 to 17.7 per cent., the latter figures being noted just before death. Eosinophile leukocytes were present in large number in the spleen, both in the sinuses and in the pulp, but eosinophile myelocytes were entirely absent. Megakaryocytes not improbably occur occasionally in the spleen of apparently healthy rodents, but none were found in the spleens of the eight guinea-pigs examined for control.

The accumulation of eosinophile myelocytes in association with other elements which are characteristic of the bone-marrow has been studied in the previously mentioned series of animals killed at varying intervals after inoculation with bacillus pyocyaneus. At the end of one-half and of one hour after inoculation no myelocytes are found. In the spleen of an animal killed at the end of two hours after inoculation an occasional myelocyte with eosinophile granulation is present in the venous sinuses. Two cells with a diameter from three to four times that of a polynuclear leukocyte are identified by their lobed or budding nuclei as megakaryocytes.

At the end of four hours the sinuses of the spleen exhibit a characteristic appearance. Within the lumen of the larger sinuses are often found ten or more cells with a diameter almost twice that of an eosinophile leukocyte; the coarse granules which stain deeply with eosin and with acid fuchsin (of the Biondi-Heidenhain mixture) are identical with those of the eosinophile leukocytes, but the nucleus of the cell is large, round or oval, and of vesicular type; one or more well-defined nucleoli are present. Similar cells undergoing karyokinetic division are found with little difficulty. The chromatin stains deeply and homogeneously and exhibits the variations characteristic of different stages of indirect division, ranging from the so-called skein formation to the diaster stage. Myelocytes with fine granulation appear to be less numerous than eosinophile

myelocytes, but are present in considerable number and at times have been fixed while undergoing indirect division. Megakaryocytes are found in the sinuses and are usually somewhat larger than those seen at an earlier stage. Polynuclear leukocytes occur in very great number, while eosinophile leukocytes with polymorphous nuclei are sparsely scattered in the tissue.

At the end of eight hours eosinophile myelocytes are present, but are much less numerous than in the spleen just described. Eosinophile leukocytes are rarely found. Megakaryocytes are present. After sixteen hours eosinophile cells have almost completely disappeared from the spleen; after twenty-four hours a small number are still present, but only one or two may be found in a single section. At this time megakaryocytes are found in considerable number.

Four hours after inoculation, at a time when eosinophile leukocytes are migrating into the peritoneal cavity and eosinophile myelocytes are numerous in the spleen, the latter may be found occasionally in the bloodvessels elsewhere. In hardened sections eosinophile myelocytes are numerous in the splenic vein and in several instances have been fixed while undergoing karyokinetic division. In a small vein of the mesentery was found one typical myelocyte.

In order to confirm the preceding observations I have studied the spleen from animals killed after infection with bacillus mucosus capsulatus and bacillus anthracis. Four hours after the injection of 0.3 c.c. of a bouillon culture of bacillus mucosus capsulatus typical eosinophile myelocytes have been found in the spleen, several not infrequently occurring in the sectioned lumen of a large sinus. Small polynuclear eosinophile leukocytes are also present in moderate number. Myelocytes with fine granulation in two instances have been found undergoing karyokinetic division, and one megakaryocyte of relatively small size has been seen.

Four hours after intraperitoneal inoculation with 0.5 c.c. of a bouillon culture of bacillus anthracis fine and coarsely granular myelocytes have been abundant in the venous sinuses of the spleen. One eosinophile myelocyte undergoing karyokinetic division has been found. Megakaryocytes are particularly numerous and vary much in size.

The occurrence of myelocytes together with megakaryocytes in the spleen a few hours after bacterial inoculation, and at a time when leukocytes both with fine and with coarse granulation are attracted in immense number to the seat of inflammation, demonstrates, I believe, that these cells have their origin in the bone-marrow and are temporarily held in the spleen. They occur in smaller number in the circulating blood. It appears probable that bacterial poisons which, Werigo and Jegunow[1] have shown, exert within from twenty minutes to an hour after inoculation a chemotactic

[1] Pflüger's Arch. f. Phys., 1901, vol. lxxxiv. p. 451.

influence upon the finely granular leukocytes of the bone-marrow, are in less degree effective in attracting from the marrow cells which are usually fixed within its substance. Myelocytes with both fine and coarse eosinophile granulation, finding their way to the spleen, are still capable of karyokinetic division, so that in the spleen and in the portal circulation multiplication of polynuclear leukocytes occurs temporarily. Eosinophile cells, both myelocytes and forms with polymorphous nuclei, have within about sixteen hours almost completely disappeared from the spleen, but megakaryocytes are still present.

Conclusions. Certain bacteria (bacillus tuberculosis, bacillus choleræ suis) producing somewhat chronic, fatal infection in guinea-pigs cause the eosinophile leukocytes to gradually disappear from the circulating blood. After death few eosinophile cells can be found in those tissues in which they are usually present in abundance. Hence the study of tissues removed at autopsy gives little indication of the behavior of the eosinophile leukocytes during the course of bacterial infections. During more acute infections produced by inoculating bacteria into the peritoneal cavity (bacillus mucosus capsulatus of Friedländer, streptococcus pyogenes) eosinophile leukocytes rapidly disappear almost completely from the peripheral circulation within a few hours.

After the inoculation of an organism (bacillus pyocyaneus), producing an infection from which the animal is capable of recovering, eosinophile leukocytes disappear from the peripheral circulation, so that their proportion may fall from 5 or 10 per cent. to less than 1 per cent. The number of eosinophile leukocytes then increases, and at the end of four or five days both the relative and absolute number of these cells may considerably exceed that present in the peripheral circulation before inoculation. At the end of six or seven days the number of eosinophile leukocytes is again normal.

When bacteria (bacillus pyocyaneus, bacillus mucosus capsulatus, bacillus anthracis) are introduced into the peritoneal cavity of the guinea-pig the large mononuclear and eosinophile cells contained in the peritoneal fluid form compact clumps which adhere in great part to the surface of the omentum, so that for a time eosinophile cells have almost completely disappeared from this fluid. At the end of about an hour they have again made their appearance. Some of the eosinophile cells normally present in the tissues of the mesentery and omentum doubtless make their way into the cavity, but soon eosinophile cells begin to accumulate in the bloodvessels of both membranes, but particularly in those of the mesentery. These cells adhere to the wall of the small veins and migrate into the surrounding tissue. This process begins about one hour after inoculation, reaches its maximum several hours later, and is more marked the larger the quantity of bacteria introduced and the more virulent

the organism employed. At the end of about four hours, when the number of eosinophile leukocytes in the peripheral circulation has undergone well-marked diminution, the same cells have accumulated in great number in the vessels of the inflamed mesentery and omentum. Similar changes are less marked below the peritoneum of the abdominal wall and below the serosa of the viscera. Though eosinophile cells are migrating from the bloodvessels into the peritoneal cavity, their relative number in the peritoneal exudate diminishes, and at the end of four hours is only 1 or 2 per cent. Polynuclear leukocytes at this time have accumulated in such immense number that they constitute an overwhelming proportion of the cells present.

Eosinophile cells are present in the cavity at the time of inoculation, but only after a period of about an hour do they begin to accumulate in increasing numbers. A primary attack of eosinophile cells such as that described by Kanthack and Hardy has not been observed. Polynuclear leukocytes with fine granulation accumulate in great quantity upon the surface of the omentum and form compact clumps held together by a network of fibrin; eosinophile leukocytes in large number penetrate into these masses of cells. Unlike the polynuclear leukocytes eosinophile cells rarely if ever, acting as phagocytes, ingest bacteria.

Eosinophile leukocytes upon the surface of the omentum, doubtless under the influence of the bacterial poisons, undergo degenerative changes of which nuclear fragmentation is the most characteristic. In such cells the eosinophile granules are still preserved. Evidence that the cells discharge these granules has not been obtained. At a somewhat later period eosinophile leukocytes are ingested by large mononuclear cells (macrophages).

Under the influence of severe bacterial infection eosinophile myelocytes together with other elements, usually regarded as characteristic of the bone-marrow, accumulate in the spleen and may be found in the circulating blood. The occurrence of this phenomenon within from two to four hours after inoculation demonstrates that these elements are derived from the bone-marrow and are not formed in the spleen. Myelocytes both with fine and with coarse (eosinophile) granulation, which have found their way to the spleen, here multiply by karyokinetic division.

Bacteria exert a chemotactic influence upon cells with eosinophile granulation, attracting them from the circulating blood to the site of inoculation and from the bone-marrow into the blood. Eosinophile leukocytes, like the finely granular polynuclear leukocytes, accumulate in the neighborhood of bacteria injected into the body and, though they rarely act as phagocytes, have a part in the series of changes which follow bacterial invasion.

THE ENVELOPE OF THE RED CORPUSCLE AND ITS ROLE IN HÆMOLYSIS AND AGGLUTINATION.

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One of the most important fields of medical research at present is that which relates to hæmolysis. The brilliant theories of Ehrlich have served to explain a large number of facts bearing on the subjects of hæmolysis and immunity. But Ehrlich's work, while it concerns itself almost exclusively with the various properties and modes of action of the biological lakers, does not sufficiently take into account the chemical, physical, and histological changes which take place in the corpuscles themselves, when these are subjected to the action of hæmolytic agents. The importance of determining as far as possible these alterations is very clear, and it is evident that only after we have an intimate knowledge of the structure of the blood corpuscles can the nature of these changes be understood.

Two theories have been advanced concerning the structure of the red blood corpuscle. According to Schäfer and others, the corpuscle is merely a vesicle and consists of an envelope which contains a fluid mass. The other—proposed by Rollet and modified by Hamburger—assumes that the corpuscles consist of a network or stroma in whose meshes are found a fluid or semifluid mass composed of hæmoglobin and electrolytes.[1]

The first hypothesis is held by very few at the present date, while the latter—which has the support of many experimental facts—is endorsed by the majority of hæmatologists. Hamburger ably discusses the latter theory and gives good reasons for its acceptance. One argument which seems particularly convincing may be quoted here: "Osmotic experiments have shown that the amount of water which a corpuscle can imbibe and give out—*i. e.*, the amount of swelling and shrinkage which it is capable of— is less than would be the case if the corpuscle were simply a vesicle. Therefore, the interior of the corpuscle must be filled up with some protoplasmic substance—a stroma or network in whose meshes is contained the water-attracting fluid of the corpuscle."[2]

As Dr. G. N. Stewart has pointed out, the presence of an envelope or limiting layer about the corpuscles seems an almost necessary assumption.[3] It is well known that there is a constant interchange of substances between the corpuscles and surrounding medium; while the metabolic products and salts within the corpuscles make their way out, these are replaced by the requisite serum constituents.

[1] Hamburger, Osmotischer, Druck und Ioneulehre, p. 171. [2] Ibid.
[3] Journal of Physiology, 1899, vol. xxiv. p. 211.

On the other hand the corpuscles keep out bodies inimical to themselves. Both of these processes which are continually going on together, and which require a selective ability on the part of the corpuscles, could hardly take place were they not provided with envelopes which permit of the entrance of some substances and the exclusion of others.

It is the principal object of this paper to adduce evidence of the existence of such an envelope and to point out the role which it plays in hæmolysis and agglutination.

The presence of an envelope may be demonstrated by histological, chemical, and physical methods.

Histological Proof. The most obvious way of demonstrating the limiting membrane of a cell is by means of differential staining, but this has proved itself to be an especially difficult method in the case of blood corpuscles. I have been able to find in the literature only one reference to a staining reaction, whereby an envelope is said to be made visible in the red blood corpuscles.

H. Deetjen[1] stains corpuscles dried on a slide and heated to a certain temperature, with gentian violet; the envelopes, according to him, are thus easily made apparent.

Dr. G. N. Stewart has published some histological plates in which is given convincing evidence of the presence of an envelope in the necturus corpuscle.[2]

In the case of some cells the envelope may be clearly seen if it be mechanically separated from the underlying intracellular substance. By this method, for instance, the sarcolemma of a muscle fibre is rendered visible.

Through a peculiar reaction which takes place when hydroxylamine hydrochlorate is added to blood, I think it is possible to produce the above-mentioned separation of envelope and cell contents in the case of mammalian red corpuscles.[3]

In this reaction bubbles of nitrogen gas are formed at the periphery of the corpuscles. These bubbles are lined externally by a delicate, apparently hæmoglobin-free membrane (Fig. 1, *a*), and internally by hæmoglobin (*b*).

The membrane is hardly stained by any of those dyes which stain the hæmoglobin in the rest of the corpuscles very deeply. This indicates that it does not contain hæmoglobin. It appears colorless in the unstained corpuscle. This might be because the color of a very thin layer of hæmoglobin might escape detection. Only by observing the corpuscles during the formative stage of the bubbles is it possible to make out that they are not formed within the hæmoglobin at all, but that the latter merely forms their inner boundary.

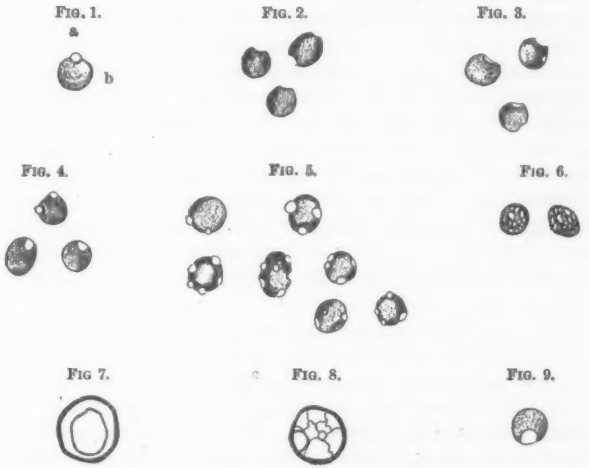
[1] Virchow's Archiv f. experimentelle Pathologie, 1901, vol. clxv. p. 232.
[2] American Journal of Physiology, 1902, vol. viii. p. 103.
[3] Peskind. Ibid., 1903, vol. viii. p. 424.

About ten minutes after the reagent and blood are mixed, the first sign of the intracorpuscular bubble formation becomes evident; it consists in a flattening or depression of the hæmoglobin on the periphery of a corpuscle, the outer lining of the bubble being too close to the hæmoglobin at this stage to be visible (Fig. 2).

The next stage is represented by Fig. 3, and shows some separation between the surface layer of the corpuscle (*a*) and the hæmoglobin.

The completed bubble appears in Fig. 4, the outer lining (*a*) often projecting considerably above the surface.

The most striking part of the reaction lies in the depression of the hæmoglobin from the surface of the corpuscle in the first stage. It demonstrates that the accumulation of gas takes place between an enveloping layer and the hæmoglobin, causing the repulsion of



the latter from the surface of the corpuscle toward the centre and, at the same time, separating the envelope from the hæmoglobin underneath.

Although gas is formed immediately on mixing the blood and reagent, yet about ten minutes elapse before bubbles are formed inside the corpuscles. This could be explained on the hypothesis that the envelope must be hardened to a certain extent before it will be sufficiently unyielding to retain the bubbles within the corpuscles.

Efforts were unsuccessfully made to produce a differential stain of the membrane-like film covering the bubbles.

Several facts will be observed in this reaction:

1. That the bubbles are lined by a delicate and very thin membrane. This, together with the observations made on the evolution

of the bubbles, renders it almost certain that the membrane lining the bubbles is the envelope of the corpuscles.

2. That the bubbles are all of small size and sharply circumscribed. This speaks very strongly for the presence of a stroma whose meshes are continuous with trabeculæ derived from the envelope; for, if the envelope were a differentiated membrane and not connected to the intracellular substance, then we would expect that the gas formed in the reaction as it collects at the periphery of the corpuscles would produce a diffuse and extensive stripping of the envelope from the contents underneath, and would not form localized accumulations or bubbles. (See Fig. 7.)

But if the envelope is part of the stroma which forms the boundary of the corpuscles, then we can readily understand how the gas accumulation would be limited to the space between the trabeculæ, thus giving rise to bubble formation. (See Fig. 8.)

CHEMICAL EVIDENCE. We come next to the consideration of such chemical facts as point to the presence of an envelope.

In a recent paper I have described a reaction between blood corpuscles on the one hand, and acids and acid salts on the other.[1] When a mere trace of most acids and acid salts is added to a suspension of blood corpuscles, the latter are immediately agglutinated and precipitated. If the corpuscles be laked, then the stromata are precipitated by the same reagents. This reaction is apparently due to the combination of the nucleoproteid of the surface layer of the corpuscles with the reagents. The reasons for this view are given elsewhere.[2]

An interesting observation in connection with this reaction throws light on the subject under consideration.

We know that all the precipitating agents—*i. e.*, acids and acid salts in dilute solution—convert oxyhæmoglobin first into methæmoglobin and then into acid hæmatin. Now if the hæmoglobin in the intact corpuscles were present in the surface layer, then we should expect it to be rapidly altered by the precipitating agents into methæmoglobin. But it was found that the hæmoglobin contained in the corpuscles was not altered in the least if the exact amount of reagent necessary to precipitate the latter was employed. Even if a moderate excess of reagent were employed in precipitating the corpuscles no methæmoglobin band appeared for five or ten minutes. However, if we lake the corpuscles first—*e. g.*, by sapotoxin or water—and then add the same amount of reagent, it will be observed that part of the hæmoglobin is instantly converted into methæmoglobin and this conversion proceeds rapidly until complete.

What is it that temporarily shields the hæmoglobin in the intact corpuscles from the action of the reagents?.

[1] American Journal of Physiology, 1908, vol. viii. p. 404.
[2] Ibid., p. 420.

Is this protection due to the fact that an intervening layer on the periphery of the corpuscle must be penetrated before the hæmoglobin can be reached, or is this conversion delayed by some chemical constituent of the corpuscles which combines with the reagent as rapidly as it enters? Such a chemical protection could be afforded to the hæmoglobin by the alkali of the corpuscles, by the stroma substance, or through the firm combination of the hæmoglobin with the stroma.

It can be shown that neither the alkali nor the stroma substance shields the hæmoglobin from the action of the reagents, since after laking the presence of stromata and liberated alkalies protects the oxyhæmoglobin but slightly and not at all if excess of reagent be present.[1]

Moreover there are many facts which suggest that the hæmoglobin compound within the corpuscle is a weak one and is easily split up.

Seeing that the temporary immunity of the hæmoglobin cannot be explained on chemical grounds, we are forced to adopt the view that there is something in the *structure* of the corpuscles, some mechanical or physicochemical barrier, which shields the hæmoglobin from the immediate action of the reagents. In other words, the hæmoglobin is protected by an envelope.

The laking of blood corpuscles by ether affords additional evidence of the existence of an envelope. It has been generally assumed that ether laking is due to the removal from the corpuscles of some or all of their cholesterin and lecithin.

This I have attempted to prove along the following lines:[2] First I determined how much ether is necessary to exactly lake 5 c.c. of blood. Then I extracted the corpuscles derived from 5 c.c. of blood with ether. The extract consisting of cholesterin and lecithin was suspended in 5 c.c. of serum or saline. Then ether was added cautiously to this suspension until the cholesterin and lecithin were perfectly dissolved and the amount of ether used noted.

It was found that the amount of ether necessary to dissolve the cholesterin and lecithin contained in the corpuscles of 5 c.c. of blood and suspended in 5 c.c. of saline or serum was about one-half again as much as was required to lake 5 c.c. of blood. So that the amount of ether required to lake blood bears a definite relation to the quantity of ether necessary to dissolve the cholesterin and lecithin of its corpuscles.

It appears from the above experiments that only a certain proportion of the cholesterin and lecithin is dissolved in ether laking,

[1] American Journal of Physiology, 1903, vol. iii. p. 422.

[2] These experiments will be published elsewhere in detail. Here I assume, in accordance with the general view, that cholesterin and lecithin are the only bodies dissolved out of blood corpuscles by ether. If, as some investigators believe, other ether-soluble substances exist, then my experiment shows that laking can be caused by the removal of other substances than cholesterin.

and this is probably the part that exists in the peripheral layer of the corpuscle. The cholesterin and the lecithin which remains undissolved during the laking in all probability remains in the interior of the corpuscle—*i. e.*, the stroma.

That the removal of lecithin alone from the envelope gives rise to laking can, I think, be readily demonstrated by the use of ether saturated with cholesterin.

If, as we have reason to believe, the cholesterin in the blood corpuscles has the same properties as the ordinary commercial cholesterin (Merck's was used in my experiments), then it would not be dissolved out from the corpuscles by ether which has been saturated with the commercial cholesterin. I found by experiment that a given amount of blood was laked by practically the same quantity of cholesterin-saturated ether as of pure ether, and, moreover, that the time required in the laking was the same in both instances.

The ether which was saturated with cholesterin laked blood just as though no cholesterin were dissolved in it. Here, I believe, we have good evidence to show that the removal of lecithin alone is capable of producing laking of the corpuscles.

Physical Proof. Dr. G. N. Stewart has made an extensive research on the conductivity of blood corpuscles. As was mentioned previously, the necessity for assuming the presence of an envelope in all animal cells became clear to him early in his experiments, and realizing this he set about to determine what changes could be produced in the envelope of the red blood corpuscles by various laking agents, using them as convenient test-objects. Unfixed corpuscles being unsuitable for various reasons, he employed formaldehyde-hardened corpuscles. Sapotoxin and sodium taurocholate when added to a suspension of formaldehyde-hardened corpuscles produced the surprising effect of greatly increasing the conductivity of the latter.

"Unhardened blood corpuscles or formaldehyde-hardened corpuscles not treated with saponin or sapotoxin permit NH_4Cl to pass much more readily into them than NaCl, and there is evidence that some of the NH_4Cl is bound by substances in the corpuscles or at any rate does not pass as freely out of them as it passes into them. After the formaldehyde-hardened corpuscles have been acted on by sapotoxin they seem to exhibit little if any power of binding either NH_4Cl or NaCl, and the ions both of NaCl and NH_4Cl wander easily through the corpuscles." [1]

It will be seen from the above that there is beyond doubt a great change in the surface layer or envelope of the corpuscles after they are acted upon by the sapotoxin.

For the purpose of determining what constituents of the formalde-

[1] G. N. Stewart, Journal of Medical Research, No. 1, vol. viii. p. 270.

hyde-hardened corpuscles are acted upon by sapotoxin the corpuscles were extracted with ether. The solvent took up a considerable quantity of cholesterin and lecithin. The ether-extracted corpuscles were carefully washed many times with salt solution and then suspended in a known volume of salt solution. For this suspension, Dr. Stewart found "the conductivity markedly greater than for a suspension of the unextracted formaldehyde corpuscles containing approximately the same proportions of corpuscles and salt solution. Sapotoxin caused no change in the conductivity of the extracted corpuscles. This renders it highly probable that sapotoxin increases the permeability of the formaldehyde corpuscles by action on the substance soluble in ether."

It can readily be shown that when a suspension of cholesterin is shaken up with sapotoxin the latter is removed by the cholesterin or rendered inert so that the liquid obtained after filtering off the cholesterin has no laking power. Apparently a definite amount of cholesterin neutralizes a certain amount of sapotoxin. I found, moreover, that formaldehyde-hardened corpuscles will also remove sapotoxin completely from a solution in twenty-four hours. So that changes in permeability produced by adding sapotoxin to formaldehyde-hardened corpuscles is clearly due to a combination of the sapotoxin with the cholesterin contained in the surface layers of the corpuscles.

While it seemed most likely to Dr. Stewart that sapotoxin exerted an action on unfixed corpuscles similar to that produced on formaldehyde corpuscles—and he gave evidence to that effect—he was unable at the time of the first research to prove this. The difficulty lay in the rapidity with which the sapotoxin causes laking. During the course of some experiments on hæmolytic agents, I made the observation that cold retards sapotoxin laking for a considerable period. This provided the means of proving the above-mentioned surmise, and to this effect a series of experiments, in some of which I assisted, were carried out. The conclusion drawn from the research are taken from Dr. Stewart's paper.[1]

1. At 0° C. the laking action of sapotoxin is much retarded, and it can be shown that before any hæmoglobin has been liberated the conductivity of the blood is increased, and presumably owing to the increase in the permeability of the corpuscles to electrolytes. At this stage sapotoxin has been fixed by the corpuscles.

2. Both at 0° C. and at ordinary temperature a dose of sapotoxin just sufficient to cause liberation of the hæmoglobin causes the discharge of a small proportion of the electrolytes of the corpuscles; when the dose is increased the electrolytes are discharged.

3. It seems permissible to divide the action on the corpuscles in three stages:

[1] American Journal of Physiology, No. 2, vol. ix. p. 96.

(*a*) An action on the envelope, which does not necessarily nor immediately lead to the liberation of the hæmoglobin.

(*b*) An action on the hæmoglobin or the stroma which causes a discharge of the pigment.

(*c*) An action on the stroma leading to the setting free of electrolytes.

Resistance of Blood Corpuscles. The so-called "resistance of blood corpuscles" affords good evidence of the existence of an envelope. "It is well known that in certain physiological states and in disease laking begins to take place in a more concentrated salt solution than is required to lake normal corpuscles. This could be due to one of several causes—either that the stroma contents of the corpuscles in disease have a greater power of absorbing water or that they possess a greater volume—or that the envelope of the corpuscles has been so altered by the disease that, when it is stretched to a certain degree, it is less able to prevent the escape of hæmoglobin than would the envelope of a normal corpuscle. That the latter is in all probability the correct explanation may be seen from the action of hæmolytic and certain bacterial toxins on blood corpuscles.

"These poisons, in very small doses, alter the corpuscles in such a manner that they cannot bear such small salt concentrations as in the normal state. This change is found to be due neither to a modification of the water-absorbing power of the corpuscular contents nor to an increase of the intraglobular volume. So that we are forced to the assumption that the hæmolytic sera give rise to a diminished resistance of the protoplasmic envelope, thus favoring the escape of the hæmoglobin when a degree of internal tension has been reached which would still leave the normal corpuscle intact."[1]

Biological Hæmolysis. Granting that the toxins of disease do cause a diminished resistance of the envelope, it is of interest to inquire whether at the same time an increased permeability of the envelope is produced. And if so, whether the corpuscle becomes more permeable to ions or to the hæmolytic agents only. It will be remembered that sapotoxin causes a primary increase in the permeability of the envelope, and by analogy one might reason that the intermediary body necessary to biological hæmolysis acts by making the envelope more permeable to the complement. In a conjoint experiment performed by Dr. Stewart and myself no evidence was obtained that dogs' serum can produce any change in the conductivity of the rabbit blood before liberation of hæmoglobin takes place.[2] This is also in agreement with the fact that the permeability of the formaldehyde-fixed corpuscles of the rabbit is

[1] Hamburger, Osmotischer, Druck und Ioneulehre, p. 391.

[2] American Journal of Physiology, No. 2, vol. ix. p. 81.

not affected by dogs' serum. Since the envelope is not made more permeable to ions by the intermediary body, it is likely that the function of the latter is to effect such changes that the complement will be able to penetrate to the interior of the corpuscle, where it can exert its specific action.

PROPERTIES OF THE ENVELOPE. The foregoing will, I think, be considered satisfactory evidence of an envelope in the red corpuscles, and we shall proceed to discuss the role that the envelope plays in hæmolysis and agglutination.

It will be appropriate at the outset to review what is known regarding the chemical and physical properties of the envelope. That it is hæmoglobin-free we have demonstrated by the action of hydroxylamine hydrochlorate and also by experiments with acid salts. (See previous pages.) That the envelope contains nucleoproteid as well as lecithin and cholesterin is shown respectively by the agglutination reaction with acids and acid salts and by the ether-laking experiments quoted previously. Alkalies must be present in combination with the nucleoproteid,[1] and salts, which always exist in protoplasm, must be contained in the envelope.

PHYSICAL PROPERTIES. The envelope of the red corpuscle appears to be smooth. That it also possesses a certain glaze I would infer from the crisp and sparkling reflex seen in fresh blood, and from the fact that the circulating corpuscles do not agglutinate with each other. This property of the envelope may subserve some defensive purpose. We can readily imagine that a corpuscle having a smooth surface will not offer so good a foothold—if the expression may be allowed—to any toxin, as would a corpuscle having a sticky envelope such as is produced by the action of an agglutinin. In support of this view we find that, as a rule, hæmolysis is preceded by agglutination. This is especially true of biological laking. In nature, wherever a biological hæmolysin occurs, there is usually also present an agglutinin in the same medium, and it seems as though the two bear a co-operative relation similar to that found between a complement and its intermediate body—which likewise are usually coexistent in nature.

When blood corpuscles are exposed to the simultaneous action of a hæmolysin and an agglutinin, the result varies with the relative strengths of the two. If the toxin be relatively weak, and the agglutinin strong, then we get primarily a powerful agglutination of the corpuscles followed by their gradual hæmolysis. If the toxin be very powerful and the agglutinin comparatively weak, then agglutination may not occur, especially if any swelling of the corpuscles is produced by the toxin. It seems that swelling of the corpuscles is inimical to agglutination.[2]

[1] Compare Hammaesten, Physiolog. Chemie, p. 80.

[2] Peskind, American Journal of Physiology, No. 5, vol. viii. p. 416.

The envelope is distensible and elastic. It is this elasticity of the envelope which permits of the expansion and shrinkage of the corpuscle brought about by osmosis. Most hardening agents do not affect the elasticity of the envelope to any degree, since after the corpuscles are fixed by these reagents they still may be caused to swell.

The envelope being protoplasmic, and therefore semifluid, must exhibit the phenomenon of surface tension. This surface tension is one of the forces which co-operate to give the corpuscles their biconcave shape. During equilibrium the intraglobular pressure must be equal to the sum of the surface tension and the pressure exerted by the liquid about the corpuscle. If for any reason the surface tension be lessened, then the intraglobular pressure could assert itself and would tend to produce a greater distention of the envelope.

Such a diminution of the surface tension in blood corpuscles is brought about, I believe, by the emulsifiers, sapotoxin and sodium taurocholate, which are known for their ability to lessen the surface tension of liquids.[1] Reasons for this view will be advanced in the discussion of the permeability of blood corpuscles.

PERMEABILITY OF ENVELOPE. A very important property of the envelope is the selective permeability with which it is endowed. A great deal of investigation has been bestowed upon this complex subject, but it still rests upon a rather unsatisfactory basis. One fact has been pretty well established, namely, that the envelope is not permeable to salt molecules but to ions only. Not all ions, however, can penetrate the corpuscles; for the most part it is the electronegative ions, the halogens and acid radicals, which have this power. The envelope is permeable for NH_4 and to free acids and alkalies, but not for Ba, Str, Ca, Mg, and in all probability it is impermeable to Na and K, although this is still under some dispute.

Of the non-electrolytes there are a considerable number which can enter the corpuscles, among which may be mentioned alcohols, aldehydes, ketone, ether, antipyrin, urea, urethane. The corpuscles are impermeable to the various sugars, but allow bile acids and salts to penetrate.[2]

One can readily imagine that the size of certain molecules may be a cause of their inability to pass through the envelope. But if the intermolecular spaces of the envelope be enlarged—as must occur when the corpuscle swells and the envelope becomes distended—then it is conceivable that some large-sized molecules could enter which, under normal circumstances, would be unable to penetrate the corpuscles.

[1] Hay's test for bile salts in urine is founded on the fact that these salts lower the surface tension of the urine.

[2] Hamburger, Osmotischer, Druck und Ioneulehre, p. 260.

Causing the corpuscle to swell is one way of enlarging the spaces which exist between the molecules of the envelope. Another method consists in removing some of the molecules which compose the envelope—*e. g.*, the cholesterin and lecithin. When these substances are extracted by ether the envelope is left in a porous condition, which makes it very permeable. This has been well shown in the experiment quoted above, in which formaldehyde corpuscles were extracted with ether. The conductivity of the corpuscles was found to be much increased by this procedure.

The suggestion may be ventured at this point that the action of sapotoxin consists partly in widening the intermolecular spaces of the envelope, making the latter more permeable to the sapotoxin molecules, which are presumably of large size. I conceive the mechanism of the process to be as follows:

First, as Ransom has shown, sapotoxin is taken up by the cholesterin of the envelope. The cholesterin and lecithin molecules are bound to the other molecules of the envelope merely by cohesion and not by firm chemical ties, since they may be dissolved out mechanically by ether. Now sapotoxin is an emulsifier, and, being such, lessens the cohesive power of fatty particles. Therefore, sapotoxin, once it has gained a foothold in the envelope, lessens the cohesion between the cholesterin-lecithin group and the other molecules which compose the protoplasm. Since surface tension is the result of the force of cohesion exerted between molecules of the surface layer, it follows that sapotoxin, in lessening the cohesion of these molecules, also lessens the surface tension of the corpuscles.

As soon as the surface tension becomes diminished the intraglobular pressure exerts itself and distends the envelope. Ions and water must now enter and the corpuscle swells.

This theoretical description corresponds very well to the actual first stage of sapotoxin laking. The corpuscles are seen to lose their biconcave shapes, become globular, and swell, showing that a great change in the surface tension has taken place, and that water and ions have entered.

At the same time it can be demonstrated that a great increase in the electric conductivity has taken place, which is probably due to the enlargement of the intermolecular spaces which accompanies the distention of the envelope.[1] The size of these interspaces being increased, the large-sized sapotoxin molecules can enter the corpuscles and split up the hæmoglobin-stroma compound, thus giving rise to laking.

Deterioration of the Envelope. The red corpuscles, like other cells of the body, are often exposed to pathological influences and suffer changes which may seriously affect their value to the

[1] It may be noted here that sodium taurocholate causes laking without any notable previous swelling of the corpuscles; the increase in the permeability produced by this reagent is also much less than that produced by sapotoxin.—G. N. Stewart.

organism. Some of these alterations are without doubt due to a deterioration of the envelope and stroma, and it will be of interest in this connection to consider under what conditions the envelope of the red corpuscles will become damaged.

The following agents may be cited as producing deleterious changes in the envelope:

1. Toxins produced in disease.
2. Chemicals—*e. g.*, acids and alkalies.
3. Drying of corpuscles.
4. Fixing blood by throwing it into boiling saline.
5. Freezing and thawing.
6. Agglutinins.
7. Aging of corpuscles.

We shall discuss these in the order mentioned.

1. *Action of Toxins Produced in Disease.* The change in the resistance of the envelope produced by hæmolysins has been considered elsewhere. A diminished resistance of the corpuscles in typhoid, pneumonia, and other diseases has been constantly observed and is in all probability due to a deterioration of the envelope caused by the specific toxins formed during the course of these diseases. Some evidence to this effect may be derived from experiments that I recently made on the sera and corpuscles of various affections.[1]

An observation, which I have made on the blood of some severe cases of anæmia and several cancer cases may be mentioned here. On exposing a drop of blood to pressure between cover-slip and slide the hæmoglobin escapes quite readily from the corpuscles. (A similar phenomenon is observed in the case of corpuscles precipitated by ammonioferrous sulphate or other acid salts.)

Hamburger[2] has shown that pressure has no effect on the resistance of normal corpuscles, so that the above observation tends to show that the resistance of the envelope had been lowered by some product of the disease.

Vacuolization. I should like to suggest here that the condition known as "vacuolization of the hæmoglobin" might be due to a localized deterioration of the envelope. Let us imagine that a very small part of the circumference of a corpuscle were injured; this would allow the very gradual escape of hæmoglobin at this point and at the same time would permit water and ions to enter so that a seeming vacuole would be produced. (See Fig. 9.)

According to this view "vacuolization of the hæmoglobin" may be considered as a localized laking of the corpuscle.

2. *Action of Chemicals.* Acids and alkalies both effect the resistance of the envelope. Corpuscles acted upon by acids give up their hæmoglobin in a weaker NaCl solution than the normal corpuscles,

[1] American Medicine, No. 23, vol. v. p. 919.

[2] Ioneulehre, p. 175.

while the contrary is the case with blood corpuscles acted upon by alkalies.[1]

3. *Drying of Corpuscles.* The effect produced on the envelopes of red corpuscles by allowing the latter to dry in air has been carefully studied by Dr. Guthrie.[2] He made the interesting observation that chickens, and human red blood corpuscles, allowed to dry in the air at room temperature, are readily laked by 0.9 per cent. NaCl solution.

It has been shown that fixing washed corpuscles by pouring them into boiling salt solution greatly increases their permeability to ions. Dr. Guthrie reasons "that a similar effect is produced by drying at a temperature below that necessary for fixation, so that the permeability of the corpuscles for diffusible substances is greatly increased, while it allows of the escape of hæmoglobin when enough water to dissolve it is present."

I have observed that when a drop of blood or of a washed suspension of corpuscles is placed on a slide and covered with a slip, those corpuscles which are at the edge of the drop—*i. e.*, where a gradual drying out occurs—become markedly swelled. And it may be demonstrated that there is also extensive laking at the edge of the drop, even in the case of corpuscles which at the moment of laking are floating in the liquid.

Dr. Guthrie in mentioning these experiments explains them very satisfactorily on the hypothesis "that the drying of a portion of the circumference of a corpuscle at the edge of the drop—or the action on it of the concentrated salt solution produced by evaporation —may render the rest of the circumference more freely permeable to the salts of the solution or to the water, and thus give rise to water laking."

4. Throwing blood corpuscles into boiling salt solution greatly increases their permeability to ions.[3]

5. Freezing and thawing causes laking, and while I have no proof to offer that this is due to an injury to the envelope, yet such an assumption seems very reasonable. The alternate contraction and expansion produced by freezing and thawing could very well have a disintegrating effect on a protoplasmic envelope consisting of heterogeneous molecules but loosely combined.

6. Agglutinins cause marked changes in the properties of the envelope, and that it also diminishes the resistance of the latter may be seen from the fact that an agglutinated mass of corpuscles loses hæmoglobin if exposed to slight pressure between slide and coverslip. Normal corpuscles cannot be laked in this manner.

7. *Aging of Corpuscles.* Old corpuscles may be distinguished in the circulating blood by the fact that they have lost a large part of

[1] Ioneulehre, p. 322.
[2] American Journal of Physiology, No. 5, vol. viii. p. 444.
[3] G. N. Stewart.

their hæmoglobin. This is most likely due to the deterioration of the envelope effected by the wear and tear to which the corpuscles are exposed.

Soon after blood is shed from an artery its permeability to NH_4Cl is greatly increased.[1] This indicates that there is a difference between corpuscles within the blood stream and those *in vitro*. It may be shown, moreover, that the envelopes of corpuscles which have been removed from the body deteriorate after a certain length of time. The behavior of corpuscles to hydroxylamine hydrochlorate may be cited as proof of this. Fresh blood, and blood less than three days old, when treated with this reagent, show bubble-formation within the corpuscles (see above). Blood that has stood for about three days will not show any bubbles with the reagent, but the corpuscles have a perforated appearance as though gas bubbles had escaped from their interior. This may be explained as follows:

Hydroxylamine hydrochlorate has a double action; not only does it permeate the corpuscles and produce gas bubbles within them, but it hardens them at the same time. If the envelope be intact, then the reagent penetrates but slowly and thus has time to harden the envelope before much of the salt enters the corpuscle. The evolution of gas produced by the reagent is thus very gradual and, as the bubbles are formed at the periphery of the corpuscle, they are retained by the partly hardened envelope. When the blood becomes old, however, the envelope deteriorates, in consequence of which the hydroxylamine hydrochlorate penetrates very rapidly, before the envelope is hardened sufficiently to be able to retain the bubbles. The result is that the reagent which enters the corpuscles in large quantities gives rise to an immediate and copious evolution of gas bubbles whose escape cannot be hindered by the weakened and only slightly hardened envelope.

The rents in the envelope produced by the escaping bubbles remain open and give rise to the perforated appearance above mentioned.

This observation shows strikingly how the envelope deteriorates with the aging of the blood corpuscles.

Hardening of Envelope. The effects of various hardening agents on the envelope and stroma are of considerable importance and merit some mention here. Among the principal hardening and fixing agents may be mentioned $HgCl_2$ (Hayem's solution), formaldehyde, osmic acid, hydroxylamine hydrochlorate, alcohol, ether, chromic acid.

In another part of the paper was brought out the fact that the distensibility and elasticity of the envelope and stroma were practically unaltered by most hardening agents, since the hardened corpuscles may still be caused to swell by suitable means.

[1] G. N. Stewart.

Agglutination of corpuscles hardened by formaldehyde, osmic acid, and ether, may still be brought about by certain means. But after fixation with $HgCl_2$ I was unable to produce agglutination. Chromic acid and picric acid agglutinate while they harden the corpuscles.

The envelopes of corpuscles hardened by formaldehyde and those hardened by $HgCl_2$ show a dissimilarity in their behavior toward sapotoxin; whereas the electric conductivity of formaldehyde-hardened corpuscles is greatly increased by sapotoxin, corpuscles hardened by $HgCl_2$ show no such effect, presumably owing to the more complete hardening produced by the latter reagent.

A peculiar effect is produced by acid salts when added to blood just shed from an artery. If to a definite amount of blood taken from the carotid and diluted with saline is added just enough ferric chloride to precipitate all the corpuscles, it will be found that the supernatant serum, after the corpuscles have settled, will not clot even after three days. This serum is neutral in reaction. The ferric chloride, combining as it does with the envelopes of the corpuscles, probably prevents the exit of the fibrin ferment, but possibly the neutralization of the alkali in the serum by the ferric chloride is the cause of its not clotting. The former mode of action is the most likely, since the addition of alkali to the serum did not produce real clotting. Further experiment must decide this point.[1]

RESUME. Various facts of a histological, chemical, and physical character show that the red blood corpuscles possess an envelope.

From the action of hydroxylamine hydrochlorate, which produces sharply circumscribed accumulations of nitrogen gas—*i. e.*, bubbles—on the periphery of blood corpuscles and not an extensive separation of the envelope from the contents underneath, it appears most probable that the envelope is not a differentiated membrane, but a part of the stroma which is condensed to form the surface layer of the corpuscle.

The envelope is hæmoglobin-free and consists of nucleoproteid, cholesterin, lecithin, and mineral constituents.

It is elastic, smooth, and apparently possesses a certain glaze which prevents the agglutination of normal corpuscles with each other and makes the corpuscles less accessible to the action of toxins.

Agglutination of blood corpuscles is due to an effect on the envelope produced by various biological products and chemical reagents whereby the envelope is made sticky.

Agglutinins, by modifying the envelope, probably lower the resistance of blood corpuscles toward toxins and other agents. From the fact that in nature they almost always occur in company with a hæmolysin, the suggestion is offered that the agglutinins

[1] American Journal of Physiology, 1903, vol. viii. p. 412.

bear some co-operative relation to the hæmolysins similar to that existing between the intermediary body and the complement, which likewise are usually coexistent in nature.

The "resistance" of blood corpuscles depends in large part upon the condition of the envelope. The latter may be caused to deteriorate by various agents principal among which are the toxins of disease. Deterioration of the envelope may be complete or partial —*i. e.*, involving the whole circumference or only a small part of the same.

So-called "vacuolization of the hæmoglobin" can be explained very satisfactorily on the assumption of a minute lesion in the envelope which allows the surrounding fluid to enter and thus permits of a localized laking at this point.

The function of the envelope is in part to make possible various metabolic processes, principal among which is the complex process known as internal respiration. This is accomplished through the medium of a selective permeability.

Another important use of the envelope is to protect the corpuscles from the action of various substances deleterious to the latter. But the very chemical constitution of the envelope may at times serve for the undoing of the corpuscles, since it has been well shown by Ransom, Kyes, Sachs, and others that the cholesterin and lecithin of the envelope fix certain toxins and thus act as intermediary bodies.

HÆMOLYSINS IN HUMAN URINE.*

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Since the epoch-making experiments of Bordet,[1] such a vast amount of work has been done upon hæmolysis and allied subjects that a review of the literature seems superfluous. For present purposes, it is only necessary to refer to some of those instances in which specific bodies have been shown to pass from the blood into the secretions or excretions.

Ehrlich and Brieger[2] showed, in the case of a goat immunized against tetanus toxin, that the specific antibody could be demonstrated in the milk. By Kassel and Mann[3] it was shown that the milk of a woman suffering from typhoid fever possessed the power of agglutinating typhoid bacilli.

Friedberger[4] was the first to demonstrate the passage of agglutinins and hæmolysins from the blood into the urine. For this purpose

* Read at the meeting of the American Association of Pathologists and Bacteriologists at New York, April 1 and 2, 1904.

he immunized a rabbit to defibrinated pigeons' blood. In conducting his experiments upon hæmolysis, he used 1 c.c. of urine from the immunized rabbit, to which were added 1 c.c. of a solution of pigeons' blood in physiological salt solution and a few drops of normal pigeons' serum. In a second experiment 1 c.c. of urine of the immunized rabbit was added to 1 c.c. of pigeons' blood in physiological salt solution, *no serum* being added. Microscopically and macroscopically merely agglutination was observed in each case. After the lapse of several hours, the cells having collected at the bottom of the test-tubes, leaving a clear fluid above, it was found that in the first experiment, to which a few drops of normal pigeons' serum had been added, the supernatant fluid was stained red, while that in the second experiment remained plainly yellow. In experiments carried out in the same manner with the urine of normal rabbits, no red staining of the fluid was obtained. Friedberger concluded from his researches that the intermediary body passed into the urine, but that the complement either did not pass into the urine or was destroyed in the urine.

Camus and Pagniez[5] are, I believe, the first to have studied the "globulicidal action" of human urine. They pointed out that the red blood cells may be destroyed in a urine (1) by virtue of its being hypotonic and (2) by the action of certain substances which isotonic or hypertonic urines may contain. Under the second group are included specific hæmolysins and other substances. They found that a normal urine, hypertonic, was at times capable of producing hæmolysis in the red blood cells of a rabbit; and this was seen to be the case only when the urine possessed a marked acid reaction. The acidity of the urine is due to the acid phosphates for the most part, to uric and hippuric acids to a smaller degree. The monobasic acid phosphate of soda in an isotonic NaCl solution gave no diffusion of hæmoglobin. Uric acid, because of its slight solubility, was not used. Hippuric acid, they say, gave positive results; after neutralization, no hæmolysis resulted. They then report pathological urines, in which the reaction was neutral or weakly alkaline, which caused hæmolysis in the erythrocytes of the rabbit; two of these were cases of chronic nephritis, the remaining two being cases of pneumonia during the period of defervescence.

Sabrazès and Fauquet[6] showed that urines, in which laking of blood did not occur, when made poor in chlorides by a rigid milk diet attained the power of laking. When the chlorides were raised to 7 grams per litre no diffusion of hæmoglobin resulted. Laking was also obtained when using the first urine of newborn infants shown to be poor in chlorides. In their experiments they added 20 c.mm. of blood to 1 c.c. of urine.

Pugnat,[7] examining urines from cases of croupous pneumonia during the febrile period, when the chlorides are greatly reduced in amount, failed to obtain laking. In each of his eight cases he

found the freezing point of the urines greater than that of the blood, and concluded that the degree of molecular concentration of a urine, as determined by the cryoscope, indicates the action which the urine will have upon the red corpuscles, laking being produced only in urines hypotonic to the blood.

The hæmolytic theory of pernicious anæmia has been ably set forth by Hunter.[8] Warthin[9] has added to it in his observations upon the hæmolymph glands in pernicious anæmia. It was with a view to determining whether hæmolysins are present in the urine in cases of this disease that the present work was undertaken. As a working hypothesis, it was assumed that pernicious anæmia is essentially the result of increased hæmolysis, which arises from the absorption of bacterial hæmolysins from the alimentary canal, the latter appearing in the urine as an excretion.

In the first place, it becomes necessary, if possible, to exclude the hypotonicity of the urines examined. To this end the cryoscope would appear at first thought to be well suited. The freezing point, however, is no criterion of the tonic strength of a urine, for the following reason: Gryns[10] has shown that solutions of urea have an action upon red blood cells similar to that of distilled water—*i. e.*, laking takes place; but urea is an influencing factor in the determination of the freezing point. A method both accurate and requiring not too much time was not obtained. Still, the estimation of the percentage of sodium chloride, the inorganic salt which is present in the urine in largest amount, will often give valuable information in cases where hæmolysis does occur. For example, if the percentage of NaCl in the urine is 0.9, one can be certain, when working with rabbits' corpuscles, that a hæmolytic action is not due to hypotonicity of the urine. In fact, percentages lower than this may be obtained, the urine still being isotonic or hypertonic, for one must not lose sight of the remaining solid constituents other than urea. The freezing point was obtained in the majority of instances, as it was often of definite aid in showing that a urine was hypotonic.

The urines examined were obtained from patients suffering with various diseases in the wards of Dr. Osler, together with urines from two obstetrical cases, for which I am indebted to Dr. Slemons, and from individuals in good health. Freshly voided samples of urine were used. For testing the urines a 5 per cent. solution of the red blood corpuscles of a rabbit was used. The blood was drawn from a vein of the ear, defibrinated, centrifugalized, and the serum was drawn off. A solution of sodium chloride, 0.9 per cent., was added. This was again centrifugalized. In all, the corpuscles were washed three times in the salt solution. A 5 per cent. solution of the rabbits' corpuscles was then made in a 0.9 per cent. solution of the NaCl. The percentage of sodium chloride in the urines was obtained by the method of Lütke-Martius.[11]

No. of case.	Diagnosis.	Hæmolysis.	Reaction of urine.
1	Typhoid fever.	—	Acid.
2	Typhoid fever (convalescent).	—	Alkaline.
3	" " "	—	Acid.
4	" " "	—	"
5	" " "	—	"
6	" " "	—	Alkaline.
7	" " "	—	Acid.
8	" "	—	Alkaline.
9	" "	+ (hypotonic).	Neutral.
10	" "	—	Acid.
11	" "	+ (hypotonic).	Alkaline.
12	" "	—	Acid.
13	" "	—	Neutral.
14	" "	—	Acid.
15	" "	—	Neutral.
16	" "	—	Acid.
17	Typhoid periostitis.	—	"
18	Croupous pneumonia (febrile).	+ (hypotonic).	Alkaline.
19	" "	+ (hypotonic).	Acid.
20	" "	—	"
21	" "	—	"
22	" "	—	"
23	Tuberculosis (lung).	—	"
24	" "	—	"
25	" "	—	"
26	" "	—	"
27	Tuberculosis (brain).	—	"
28	Tuberculosis (peritoneum).	—	Alkaline.
29	" "	—	Acid.
30	Tuberculosis (intestines) (atrophic cirrhosis of liver).	—	Neutral.
31	Bronchial asthma.	—	Acid.
32	Influenza.	—	"
33	Pleurisy with serous effusion.	—	Neutral.
34	" " " "	—	Acid.
35	Pleurisy.	—	"
36	Amœbic dysentery.	—	Neutral.
37	" "	—	Acid.
38	Dysentery (bacillary ?).	—	"
39	Catarrhal jaundice.	—	Alkaline.
40	" "	—	Acid.
41	Obstructive jaundice (gallstones).	—	"
42	" gallstones.	—	Neutral.
43	Chronic jaundice (cause ?).	—	Acid.
44	Hypertrophic liver cirrhosis.	—	Neutral.
45	Acute rheumatic endocarditis.	—	"
46	" " "	—	"
47	Chronic endocarditis.	—	Alkaline.
48	" "	—	"
49	Myocarditis.	—	Acid.
50	" and arteriosclerosis.	—	"
51	" and angina pectoris.	—	"
52	Mitral insufficiency and stenosis.	—	Neutral.
53	Aortic " neurasthenia.	—	Alkaline.
54	" " aneurysm.	—	Acid.
55	" "	—	Alkaline.
56	" "	—	Acid.
57	Thoracic aneurysm.	—	"
58	Pericarditis with effusion.	—	"
59	Acute articular rheumatism.	—	Neutral.
60	Gon. rrhœal arthritis.	—	Acid.
61	Arthritis deformans.	—	"
62	"Still's disease."	—	"
63	Spondylitis.	—	"
64	Transverse myelitis (acute).	—	Alkaline.
65	Syphilis.	—	Acid.
66	" aneurysm.	—	"
67	" (congenital).	—	"
68	Basedow's disease.	—	Alkaline.
69	Neurasthenia.	—	Neutral.
70	"	—	Acid.
71	"	—	Neutral.
72	"	—	Alkaline.
73	"	—	Acid.
74	Anorexia nervosa.	—	"
75	Chronic interstitial nephritis.	—	"
76	" " "	+ (hypotonic).	Neutral.
77	" " "	+ (hypotonic).	Acid.
78	" " "	—	"
79	Chronic interstitial and parenchymatous nephritis.	—	Alkaline.

No. of case.	Diagnosis.	Hæmolysis.	Reaction of urine.
80	Hæmatoma of kidney.	—	Acid.
81	Diabetes mellitus.	—	Alkaline.
82	" "	—	Acid.
83	" "	—	"
84	Uncinariasis.	—	"
85	Splenomyelogenous leukæmia.	—	"
87	Henoch's purpura.	—	"
88	Polycythæmia.	—	"
89	Pernicious anæmia I.		
	Examination *a*.	+ ($\Delta = -1°.805$)	"
	" *b*.	—	"
	" *c*.	—	"
90	Pernicious anæmia II.		
	Examination *a*.	+ (NaCl = 0.7605 %)	"
	" *b*.	+ (NaCl = 0.6903 %)	"
	" *c*.	+ (NaCl = 0.6318 %)	"
	" *d*.	—	"
	" *e*.	—	"
91	Pernicious anæmia III.		
	Examination *a*.	+ (NaCl = 0.5031 %)	"
	" *b*.	—	"
	" *c*.	+ ($\Delta = -0°.61$)	"
	" *d*.	—	"
	" *e*.	—	"
	" *f*.	+ (NaCl = 0.74 %)	"
	" *g*.	—	"
92	Pernicious anæmia IV.		
	Examination *a*.	+ ($\Delta = -0°.916$)	"
	" *b*.	—	Alkaline.
	" *c*.	—	"
	" *d*.	—	"
93	Pregnancy.	—	Acid.
94	Puerperal eclampsia (6 examin.)	—	"
95	Healthy individual.	—	"
96	" "	—	"
97	" "	—	"
98	" "	—	Alkaline.
99	" "	—	Acid.
100	" "	—	Alkaline.
101	" "	—	Acid.
102	" "	—	"
103	" "	—	Neutral.
104	" "	—	Alkaline.
105	" "	—	Acid.
106	" "	—	"

The above table will serve to show partially the results obtained. The sign + denotes hæmolysis, the sign — its absence.

The experiments were conducted in small test-tubes, after Friedberger, in the following manner:

Experiment A. Ten drops of urine; ten drops of a 5 per cent. solution of rabbits' corpuscles; three to four drops of normal rabbits' serum.

Experiment B. Ten drops of urine; ten drops of a 5 per cent. solution of rabbits' corpuscles.

The test-tubes, after having been filled, as above, were placed in an incubator at 37° C. for two hours. They were then placed in a temperature of 0° C. for about twenty hours. The tubes were then examined macroscopically and spectroscopically. In all cases where sedimentation was not satisfactory, the contents of the test-tubes were centrifugalized. The supernatant fluid was in each instance examined with the spectroscope for the bands of oxyhæmoglobin.

From the foregoing table it is seen that in no instance, except in cases of pernicious anæmia, was hæmolysis obtained where hypotonicity could be excluded. The results in the cases of pernicious anæmia require further explanation.

Solutions of sodium chloride of various strengths were prepared in which rabbits' corpuscles were suspended. The solutions were placed in test-tubes which were put in the incubator, and later in the refrigerator; in fact, treated exactly as in the experiments described above. A 0.66 per cent. solution of sodium chloride showed no diffusion of hæmoglobin from the rabbit's corpuscles, while hæmoglobin was present in the supernatant fluid in a 0.64 per cent. solution. Thus it is seen that in case No. 90, examinations *a* and *b* and in Case No. 91, examination *f*, the positive result may not be explained on the ground of hypotonicity. Again, it must be kept in mind that in the experiments ten drops of urine were added to ten drops of a 0.9 per cent. solution of NaCl; so that in each case where percentage of NaCl is recorded the resulting strength in sodium chloride is above 0.7 per cent. None of the pernicious anæmia urines showed the bands of oxyhæmoglobin on examination previous to the addition of the solution of rabbits' corpuscles.

In all cases where hypotonicity could be proven to exist, the supernatant fluid took on a deep-red color soon after the addition of the rabbits' red blood cells. This was the case in none of the pernicious anæmia urines. In no instance did the supernatant fluid show a marked pink color in this disease. On the contrary, only the suggestion of a pink color was to be seen. But in each case recorded as positive, the bands of oxyhæmoglobin were present on spectroscopic examination. In each of the examinations designated as positive, the fluid in experiment A was perceptibly darker than that in experiment B, and, in the former, the spectroscopic bands of oxyhæmoglobin were darker. In no case was this observed in any of the hypotonic urines. This fact convinces me that coloring of the fluid was not due to hypotonicity of the urine. If this were the case, why should twenty drops of a hypotonic solution, to which three drops of normal rabbits' serum has been added, show greater diffusion of hæmoglobin than twenty drops of the same solution to which no serum was added? The darker coloring in the tube to which normal serum was added coincides with Frieberger's results, although it seems that some complement is present in the urine.

No results were obtained comparable to those of Camus and Pagniez in working with normal urines. In every instance where diffusion of hæmoglobin took place, excepting the cases of pernicious anæmia, hypotonicity was proven to exist. It is to be regretted that details of their experiments are so meagre. In the cases of pneumonia, in which they report hæmolysis to have been present, neither freezing point nor percentage of chlorides is given, so that one cannot judge of the tonic strength of the urines.

The presence of hæmolysis in the urines of the pernicious anæmia cases has, so far as can be seen, no definite relationship to a rising or falling number of red blood cells. The observations extended over too short a space of time, however, to answer this point satisfactorily.

The fact that hæmolysis was not found constantly in the urines, that it was present at one examination, absent in the next, would seem to support Warthin's[9] theory as to the cyclical or intermittent nature of the hæmolysis in this disease, though one cannot deny that this may be due wholly to temporary changes in the excretory power of the kidneys irrespective of other changes in the organism.

The possibility of pernicious anæmia being due to the absorption of bacterial toxins is clearly set forth by Hunter.[8] Elders[12] reports a case treated successfully by antistreptococcus serum which supports Hunter's view. Welch[13] mentions the possibility of "certain obscure anæmias" being due to the absorption of toxins of bacteria. It is possible that the hæmolysis found in the urines of pernicious anæmia is due to bacterial hæmolysins which have been absorbed, though hæmolysins from other sources cannot be excluded.

It is my pleasure to thank Professor Osler for his kindness in facilitating the work; also Dr. Emerson, the director of the clinical laboratory.

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MENTAL SYMPTOMS ASSOCIATED WITH PERNICIOUS ANÆMIA.

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THE spinal cord lesions and symptoms of pernicious anæmia, through the work of Lichtheim, C. W. Burr, and others, have become an old story, of which the sequel, written by Putnam and

Taylor, and others, reveals the probable role of anæmias and cachexias in a large group of combined degenerations of the cord.

Mental symptoms of the character of delirium and confusion in pernicious anæmia were early recognized. "The mind occasionally wanders," said Addison, in his classic portrayal of idiopathic anæmia,[1] and subsequent writers have, in similar comments, noticed mental disturbance as a terminal incident in this grave blood disease. A Swedish observer, Henry Marcus, in the *Neurologisches Centralblatt*, May 16, 1903, describes a psychosis resembling expansive paresis, but associated with anæmia which he designates as "pernicious," although the lowest blood estimation was 2,400,000 red cells and 27 per cent. hæmoglobin; while no differential count of leukocytes is published and no mention is made of nucleated red cells. The mental symptoms in Marcus' case subsided in the course of six months with very little improvement in the blood state, and had not returned two years later, which I think is the strongest support for his claim that this was a true pernicious anæmia—psychosis.

Yet, I have seen the wildest delusions of grandeur fade in a few weeks, giving place to a remission of four years' duration, apparently, and as the late D. E. Hughes believed, through the correction of a simple anæmia; and I have seen paretic symptoms lighted up by alcoholic debauches at three periods about a year apart, to fade again as the alcoholic influence was eliminated in the first and second accesses, but apparently to become established in the third access, the patient appearing then as a confirmed paretic. It would seem that these toxic states belong in the category of exciting causes of paresis along with trauma and the puerperium; and so it is possible that Marcus' patient is a paretic after all.

Secondary anæmias are found in association with various mental states. About two years ago it occurred to me that cases of paresis in which the cord succumbs to the disease first might show a peculiar blood state as compared with those in which mental symptoms usher in the disease; and I made blood examinations of 7 cases of paresis of the spinal type in order to compare them with the ordinary cases which might be called, in view of the studies of Storch and of Schaffer, the *forebrain* type.

Assuming that the cases studied by Capps in 1896[2] and by Jelliffe in 1897[3] belong mainly to the latter or ordinary type, the comparison of the two types appears as follows:

[1] Osler, in his Practice, quotes all that Addison said of the disease.
[2] The American Journal of the Medical Sciences, June, 1903.
[3] New York State Hospital Bulletin, July, 1903.

Name.	Station and gait.	Knee-jerks.	Pupils.	Light reaction.	Accommodation.	Red corpuscles.	White corpuscles.	Hæmoglobin.	Polymorphonuclear	Lymphocyte.	L. mononuclear.	Eosinophiles.
9	.....	.....	.....	.....	.....	3,700,000	21,066	65 %	69 %	19 %	5 %	7 %
W. M.	Very poor, paraplegia.	Absent.	Large; right larger.	Both good.	Good; nystagmus.	3,260,000	25,400	50 %	53 %	12 %	29 %	6 %
J. F. B.	Moderate ataxia; weakness.	Very quick.	Right larger.	Absent.	Poor; horizontal nystagmus.	3,380,000	14,400	70 %	54 %	40 %	4 %	2 %
G. R.	Moderate ataxia; weakness.	Absent.	Fairly large; right slightly larger.	Absent.	Good.	2,820,000	24,000	80 %	95 %	4 %	1 %	0 %
H. D.	Poor station; ataxic gait.	Absent.	Small; right larger.	Both slight.	Better than light.	3,800,000	22,933	65 %	53 %	35 %	12 %	0 %
H. M. D.	Ataxic gait.	Plus; ankle clonus.	Large; left larger.	Left none; right good.	Both good.	4,240,000	32,533	72 %	68 %	24 %	7 %	1 %
C. H.	Ataxic gait.	Plus.	Pinpoint; left larger.	Both slight.	Sluggish.	3,580,000	36,266	60 %	69 %	20 %	8 %	8 %
	Spinal type (averages of above)					3,516,000	25,922	66⅙ %	65⅓ %	22½ %	10⅓ %	2 %
	Ordinary type (averages in 19 cases reported by Capps)					4,789,774	12,233	84⁹/₁₀ %	75½ %	14¼ %	7⅞ %	2½ %
	" " (in Jelliffe's 18 cases)					5,714,333	7,106	88 %	73⅗ %	16⅗ %	7⅕ %	1⅘ %

If we may draw a conclusion from this small series of cases, it is this: When the spinal cord bears the brunt of the disease process in paresis, a simple anæmia with leukocytosis is found; when mental symptoms alone appear, the blood state is not characteristic. Perhaps anæmias or the toxins of anæmias are a factor in the cord lesions even of paresis.

My cases were, mentally, early ones, yet the blood counts resemble those obtained by Diefendorf[1] in the last stage of ordinary paresis; so it may be that simple anæmia with leukocytosis is merely a consequence of advanced paretic degeneration, whether this be spinal as in my cases, or cerebral as in Diefendorf's.

The frequency of spinal-cord involvement in pernicious anæmia is evidently great; diffuse degenerations occur even when spinal symptoms are not apparent; tract degenerations have been traced by Spiller and others into the brain stem; but of cerebral lesions from pernicious anæmia nothing of value is known. I hope to report upon this point later, as I have two brains from cases in which the blood state was extreme, and mental symptoms prominent; and Professor Coplin has a third brain from a case in which I have been interested medicolegally, since the individual's testamentary capacity was called in question by reason of mental disturbance that arose in the last month of his life.

Dr. E. Q. Thornton has furnished me with notes of this case: A merchant, aged fifty-five years, consulted Dr. Thornton on November 12, 1902, complaining chiefly of languor, but appearing of such a bad color that he was sent for a blood examination at once to Dr. Rosenberger, who reported the following: red corpuscles, 1,500,000; white corpuscles, 7500; hæmoglobin, 35 per cent. Poikilocytosis; large and small nucleated red cells.

On January 25, 1903, the man took part in an interview that agitated him; the next day his temperature rose to 103° F. and he became delusional, declaring that his wife was trying to poison him; that she was unfaithful and that the nurses and doctors were in a conspiracy with her to get his property; he exhibited his hands from which "poison" was exuding; described disagreeable odors of poisonous gases, and attempted to escape by the windows repeatedly. He disinherited her by tearing up a will made in her favor long before. Yet he was not much disoriented and could talk clearly of other matters. Death occurred on February 18, 1903.

Lena P. was an inmate of the Insane Department, Philadelphia Hospital, for twelve years; she had pernicious anæmia on admission in 1890; a blood count made by Dr. Gilmore at that time showed red corpuscles, 590,000. She died of the disease in 1902. The blood count four days before death was: red corpuscles, 1,107,000; white

[1] The American Journal of the Medical Sciences, December, 1903.

corpuscles, 9166; hæmoglobin, 18 per cent. Macrocytes, microcytes, gigantoblasts, and normoblasts.

She had the color and other evidences of the disease throughout the entire period, and was mildly demented; but she was subject to exacerbations of the blood disease—in a number of which blood counts were recorded—and at the same time of her mental symptoms becoming dreamily confused.

Catharine McB. was brought to the Philadelphia Hospital from the House of Correction, in a state of confusion with excitement—a mild delirium. Examination of the blood revealed the following: red corpuscles, 690,000; white corpuscles, 12,000; hæmoglobin, 15 per cent. Marked poikilocytosis, many macrocytes and microcytes, normoblasts and gigantoblasts.

Michael F. was sent to the Philadelphia Hospital by Dr. J. O. W. Kelly, on account of a hallucinatory confusional state, of three months' duration. The patient's color and weakness suggested to the late Dr. Hughes a blood disease, which was found: red corpuscles, 2,990,000; white corpuscles, 11,466; hæmoglobin, 38 per cent. The man cleared mentally and left the hospital after five weeks of treatment, although he was still anæmic.

Bessie M. is at present under treatment at the Philadelphia Hospital Insane Department. The blood count is: red corpuscles, 3,230,000; white corpuscles, 28,133; hæmoglobin, 55 per cent. Normoblasts and gigantoblasts are abundant. The mental state, as much as the color of the skin, suggested pernicious anæmia in her case.

A composite picture of the mental disturbance in these cases presents a shallow confusion with impairment of the ideas of time and place (disorientation), more marked on awakening from sleep. The patient fabricates, relating imaginary experiences of "yesterday" in a circumstantial way.

Illusions, particularly of identity, are common. Hallucinations appear at times, pertaining to any of the senses.

Based upon these illusions and hallucinations, persecutory delusions arise. These are usually transient, causing episodes of fear and agitation, but they may persist for considerable periods and be thus somewhat fixed; they may be even systematized, as in Dr. Thornton's case.

The pernicious anæmia psychosis is mainly an abeyance of mind; it rarely presents that spontaneous excitement by which some types of confusion seem to merge into true mania; so that the term amentia, in Meynert's sense, seems appropriate for it. Of Meynert's two groups, *idiopathic* and *symptomatic* amentia, the latter, of course, would embrace the pernicious anæmia psychosis. Korsakoff's disease and folie Brightique resemble it closely.

CLINICAL AND HISTOLOGIC STUDY OF THE OPHTHALMIC CONDITIONS IN A CASE OF CEREBELLAR NEOPLASM OCCURRING IN A SUBJECT WITH RENAL DISEASE.[1]

By Charles A. Oliver, A.M., M.D.,
of Philadelphia.

In the month of February, 1898, A. C. T., a white woman, aged forty-eight years, married, and the mother of one living child, came under the care of Dr. J. Hendrie Lloyd in the Wards for Nervous Diseases at the Philadelphia Hospital. Dr. Lloyd's most careful notes of the case state that the principal complaints of the patient upon her admission into the hospital were double vision "with incomplete loss of vision in the left eye," and weakness in the legs and lumbar region. The patient's family history showed that both her father, a man aged seventy-nine years, and her mother, a woman aged sixty-nine years, were living. The patient was one of thirteen children, of whom four brothers and four sisters were living; of the remaining four children, all brothers, two died during infancy; the third in adult life (from hypertrophic cirrhosis of the liver), and the fourth from some unknown cause.

The patient had had "all of the diseases of childhood." She first menstruated at twelve years of age, and had been "regular" up to her forty-sixth year of age, the epochs usually lasting for three or four days' time. The flow was always moderate in quantity, and the crisis was never painful. Menopause had been slowly though undisturbingly establishing itself for the past two years. She had one living healthy child. She never had any miscarriages. Seven years before admission she had suffered from an attack of acute articular rheumatism, followed four years later by inflammation of the lungs. She reported that she had never had venereal disease, and she had never had any gross accidents or operative interference. She had never used alcohol or tobacco.

She said that following her recovery from the pneumonia she suffered from occipito-vertical pains and vomiting at each premenstrual period, the headache having ceased during the last eight attacks, but the vomiting being preceded by gross exacerbations of nausea. She stated that she had been unable to walk without assistance for three years' time. For two years she had had "weakness in the lower part of the back." There was frequent desire with difficulty in micturition, the patient not always being able to urinate. There had never been any retention or incontinence of

[1] Read before the March, 1904, meeting of the Section on Ophthalmology of the College of Physicians of Philadelphia.

urine. Her bowels had been constipated much of the time for fully a year.

Four weeks before she was seen she had experienced a severe attack of nausea and vomiting which had lasted for three days' time. Just previous to this attack she had had so much dizziness as to cause her to fall from a chair. After this accident she noticed that objects appeared double and that she was told at times that her eyes seemed crossed. At this time vision with the left eye began to fail. These symptoms were almost immediately followed by loss of vision in the left eye. The vertiginous seizures persisted, though to a much less degree, while the patient was placed in a prone position.

Upon admission to the hospital, the patient appeared to be well nourished. Her radial pulse was 100, small and compressible. Her heart sounds were rapid, the second beat being accentuated. The tongue was protruded straight, and there was not any marked tremor. There was not any trembling of the lips. The masseter, the temporal, and the pterygoid muscles acted well. Neither the sensory nor the motor portions of the fifth nerve seemed involved. A slight trembling of the hands and arms upon extension was noticeable. Hand grip was equally good on both sides. Sensation and localization were good in both arms. The biceps jerks were apparent. The patellar tendon reflex was exaggerated on the right side, and ankle clonus was absent on both sides. The plantar reflex was increased, while sensation in the legs was somewhat greater than normal. Pressure upon the sacral region gave rise to tenderness. Station was poor, while gait was slightly ataxic in character. There was marked inco-ordination. Examination of the urine gave a low specific gravity, a minor amount of albumin, and the presence of a few granular and hyaline casts.[1]

The pupil of the right eye was 1 mm. larger than that of the left, which was 4 mm. wide in the horizontal meridian. Iris reactions to light stimuli were very feeble, and were not so good in the left eye as in the right one when gross attempts at accommodative efforts were made. A medium degree of paresis of the left external rectus muscle, together with a slight paresis of the corresponding orbicularis muscle, could be determined both objectively and subjectively. There was imperfect action of the muscles which were supplied by the left oculomotor and pathetic nerves.

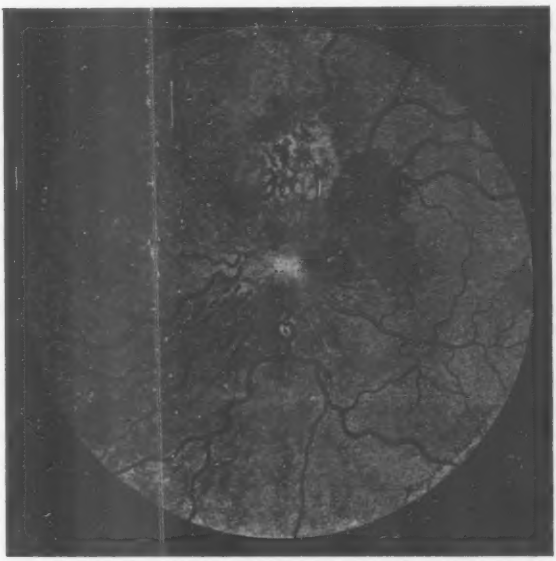
The ophthalmoscope showed that there was a marked degree of neuroretinitis, the swollen tissues of the left optic nerve-head being denser and more extensive than those of the right eye (seven dioptres as compared with six dioptres for the right optic nerve-head swelling). There were numerous superficial and deeply seated hemorrhages in both the neural and retinal tissues, particularly along the

[1] For a most interesting and instructive difference between these findings and those of the urine which had been examined eight years previously, see later notes in report of this case.

larger temporal vessels. Great numbers of commencing degeneration areas could be seen in both papillomacular regions, though more pronounced in the left eye.

Uncorrected vision with the right eye equalled one-third of the normal, this being improved to one-half of normal by having the patient gaze through a pinhole. Vision with the left eye was one-sixth of normal, being brought to one-fifth by use of the pinhole. The visual fields were lessened somewhat concentrically with the presence of great numbers of mutable relative and absolute scotomatous areas with fixed enlargements of the physiological blind

FIG. 1.



Ophthalmoscopic appearance of left eye-ground.

spots. There was not any accommodative play, the one-half dioptre type being clearly and fixedly defined at 30 cm. when looked at through a convex spherical lens of four dioptres' strength with the right eye, and the three-quarters of a dioptre type being seen clearly at 25 cm. distance with the same correcting lens. Intraocular tension in each eye was normal.

The ticking of a watch, which could be heard at 30 cm. distance from the right ear, was not audible even when the watch was held close to the left ear.

Upon re-examination of the ocular conditions eleven days later it

was found that the patient was unable to make use of the lower fibres of the left orbicularis muscles, the upper fibres, and particularly those in the unstriated series at the inner angle, being but slightly contractile, with compensatory movement of the globe, given in order to place the cornea beneath the upper lid.

Ophthalmoscopic examination of both eye-grounds as pictured in the accompanying sketch (Fig. 1) of the left eye-ground, made by Miss Margaretta Washington, of this city, showed fresh hemorrhages, both superficial and deep, in the retinal tissues. The swelling of the optic disks had subsided to about two dioptres, and the tissues of the nerve-heads had become much thickened. The retinal plaques and patches noted in the previous study still existed.

In the lower part of the superficial layers of the left cornea there was a large saturated and markedly anæsthetic ulcerous area, which was rapidly extending into the corneal layers, giving rise to an extreme irritability of the eyeball. The conjunctival membrane, particularly that portion of it which was situated in the neighborhood of the ulcerous spot, was proliferating its external squamous cells, and there was a corresponding desquamation of the neighboring epithelium. The previous convergence was now noted as having become bilateral, this being produced by a paresis of the right external rectus muscle, though to a lesser degree than that of the left eye.

At this time the patient voluntarily gave the information that for the first time she had experienced attacks of irritation phosphenes in the shape of golden rain, which was situated directly in front of the right eye. The visual fields both for form and color were lessened irregularly to a greater degree than they had been at the earlier examination. Intraocular tension had become slightly diminished in the inflamed eye. Vision with this eye had decreased to an uncorrectable one-thirtieth of normal.

From this time on vision in both eyes steadily failed until she became practically blind; postneuritic changes set in; muscle palsies of the most bizarre types appeared; and the general condition gradually weakened until in some six weeks' time after she had been first studied she died from apparent uræmic poisoning.

A most careful autopsy was made. The scalp and the calvaria did not present anything abnormal. The dura mater was not especially adherent. There was not any excess of fluid in the subarachnoid spaces. The small vessels of the pia mater were injected, and the large ones were distended. The membrane itself was almost transparent.

Springing from the left lobe of the cerebellum was a cone-shaped mass which proved to be sarcomatous in character. The apex of the growth was nipple-shaped and projected forward to a point which was situated slightly anterior to the middle line of the pons

varolii and reached to within 1½ cm. of the origin of the left crus cerebri. The base of the tumor was found to be placed somewhat anterior to the middle of the left cerebellar hemisphere. The tumor-mass was 3 cm. broad at its base; its total length was 55 mm., and its greatest width was 33 mm. Laterally, toward the median line, the growth pressed upon the medulla oblongata, while on the left side it rested upon the posterior part of the pons varolii. The medulla, which was flattened laterally, was twisted on its longitudinal axis in such a manner that it was directed at an angle of forty-five degrees away from the median line, causing its normally placed left lateral surface to be turned obliquely upward. The growth was sharply circumscribed and could be readily removed from the cerebellum. Its posterior aspect was covered by pia mater, while its anterior face was possibly similarly conditioned.

The mass, which was firm in consistency, had an irregularly convoluted surface, resembling that of brain tissue. Upon section, it was yellowish-red in color and exhibited a few distended vessels and small free hemorrhages.

The seventh and eighth nerve trunks on the right side appeared to be in good condition, while the corresponding left ones were swollen and indistinct. There was a marked softening of the pons varolii in the position where the neoplasm pressed upon it. This softening extended to about 2 cm. in advance of the growth. The tumor was adherent to the base of the skull.

After removal of the brain it was found that the posterior part of the petrous portion of the temporal bone was deeply eroded. The cavity made by the growth was 2 cm. long, 14 mm. wide, and 1 cm. deep. The central part of this excavation corresponded in position to that of the internal meatus. The bone surface in the excavated area was rough and was crossed by a series of serrated elevations. The cavity was filled with soft tumor-like masses of reddish tint.

The body was emaciated. The cæcum and ascending colon were distended with gas. The appendix was bound to the cæcum and the ascending colon by adhesions. The pleuræ were free. Both the right and left lower lobes of the lungs were somewhat congested, while the upper lobes were slightly emphysematous. There were a few adhesions between the lobes of the left side. The pericardium showed a great deal of fatty infiltration. The heart muscles were some 18 mm. thick. Both the aortic and the pulmonary valves were normal; the tricuspids were thickened. The mitral valve exhibited a few yellowish opaque spots. The liver was small, its right lobe being 19 cm. long and its left lobe 16 cm. long; its average thickness was 4¾ cm. The gall-bladder projected for some 5 cm. beyond the surface of the liver. There was a slight increase of connective tissue between the lobules of the organ. The interior of the aorta was both roughened and thickened. The spleen was small, very dark in tint, and quite soft. The pancreas did not pre-

sent anything abnormal. The left suprarenal capsule showed fatty degeneration in its cortex. The capsules of both kidneys could be stripped with difficulty. The organs themselves were somewhat smaller in size than normal. Their cortices, which were red in tint, were reduced in thickness. The pyramids were fibroid in character. The pelvic membranes were injected, those of the left kidney being infiltrated with pus. The bladder was contracted; its walls were greatly thickend, and its cavity was filled with pus.

The posterior halves of the eyes, together with the orbital portions of the optic nerves, were removed and placed in formalin.

Some few months later, while inspecting some notes in my clinical service at Wills Hospital, I unexpectedly came across a carefully prepared record of this patient who had visited my out-patient service in December, 1890. The symptoms complained of at that time were typically those of renal disease. The ophthalmic examination, which was most complete, showed the presence of some faint star-like degeneration radii in both macular regions, with a few superficial and deeply seated hemorrhages in the papillomacular areas, in association with a small mosaic of pigment aggregations with intervening fatty degenerations, slightly down and out from the left optic nerve-head, and extending into the macular region. Vision with the right eye was reduced to four-fifths of normal and to two-thirds of normal with the left eye. The visual fields were large. They presented proper color sequences and were well shaped; small but negative central scotomas being present. Examination of the urine at that time revealed a fluid of good specific gravity, but containing a faint trace of albumin and some granular casts. The patient, who was ordered an appropriate regimen and was given a prescription for Basham's mixture, failed to return after the third visit.

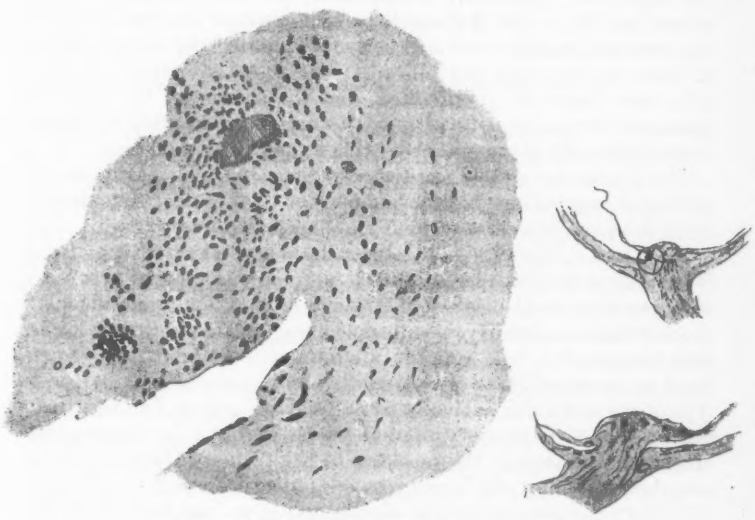
Through the kindness of Dr. Edward A. Shumway of this city, the left eyeball was embedded in celloidin, and sections were made through the optic nerve and neighboring ocular tunics.

Macroscopically, the optic nerve was much thinner than ordinary, and its intraocular extremity showed decided swelling.

Microscopically, the optic nerve-head was found to be swollen, the result of the swelling being $\frac{87}{100}$ mm. above the level of the lamina vitrea of the chorioid. The tissues were infiltrated with a great number of cells which had assumed spindle-like forms; these cells being particularly numerous around the vessels, forming complete mantles in places. (*Vide* sketch by Dr. Ellen C. Potter, Resident Physician at the Woman's Hospital of Philadelphia). In those sections which were stained by the Van Gieson method, the intercellular substance stained with fuchsin, and appeared to be composed of fine connective-tissue fibres (by the contraction of which the optic nerve fibres had become atrophic, as no trace of them could be found). The vessel walls were very much thick-

ened and the lining endothelial cells were proliferated, but the chief increase in thickness was situated in the adventitia. Embedded in the swollen nerve-head were several irregularly round bodies, staining faintly pink with eosin, and light red with the Van Gieson reagents. These bodies were without structure, and resembled those which are found in the nerve-head in senile conditions of the eye. Similar formations were also found in the intervaginal space. The fibres of the lamina cribrosa were thickened and extended further forward than usual. Posterior to the lamina cribrosa, on the temporal side, the intervaginal space was widely distended, and the cavity thus formed, which extended backward for a distance of

FIG. 2.



Spindle-like cells around vessels in swollen optic nerve-head.

1 mm., was filled with a loosely coagulated fluid and crossed by swollen connective-tissue processes. Everywhere else the space between the dural and pial sheaths was filled with a mass of proliferating cells. These cells were similar in type to the endothelial cells that line the processes of the arachnoid. In consequence of these changes, no lymph space existed around the optic nerve. The connective-tissue septa within the optic nerve were normal in thickness and were moderately infiltrated with lymphoid cells —particularly around the central vessels. The decrease in the diameter of the nerve was due to an almost complete atrophy of the nerve fibres. With the Weigert sheath stain only an occasional

tenuous thread, continuing for a short distance to end in a minute globule, could be seen.

The retina exhibited circumpapillary inflammation and œdema. The changes were situated chiefly in the outer layers, and consisted in hypertrophy of the supporting elements, their separation by fluid, and the formation of cystic cavities.

In one place (the macular region) there was a mesh-like deposit of fibrin, such as is common in retinitis albuminurica. Swollen, fatty cells were occasionally seen, but no hemorrhages could be found. The rods and cones were degenerated, their outer ends being converted into irregularly shaped masses. The fibre layer of the retina showed œdema and hypertrophy of the supporting fibres, but there were not any large cavities. The nervous elements in this layer had apparently disappeared, no fibres could be determined, and but a few of the cells present could be isolated as highly degenerated ganglion cells. The vessels showed the same changes as those in the optic nerve-head. The so-called retinal pigment cells were decidedly proliferated, and the surface of the chorioid presented several masses of partially organized exudate to which some of the cells of the outer retinal layer remained adherent.

The chorioidal vessels were widely distended with blood, which contained numerous polymorphonuclear leukocytes; the stroma being moderately infiltrated with mononuclear round cells.

Remarks. The case is of interest from several standpoints: the formation of a cerebellar tumor of sarcomatous type in a subject with previous renal disease; the existence of a low grade macular chorioretinitis in both eyes, with the characteristic ophthalmoscopic phenomena of a true retinitis albuminurica without any coarse signs of endarteritis or perivasculitis eight years before the gross type of neuroretinitis, which is so peculiar to increased intracranial pressure, and particularly to that which is found in subtentorial neoplasms, appeared; the masking of the primary changes in the macular regions by the later gross ones of neuroretinitis with their post-mortem exposure by the microscope (*i. e.*, the finding of the solitary remnant of the previous localized retinal and chorioidal inflammation from disturbance in the vascular network—the mesh-like deposit of fibrin); the final rapid loss of vision in so brief a period of time (three months) (the reason for which was so well shown post-mortem by the almost, if not quite complete, atrophy of the nervous elements of the retina and the optic nerve); the disappearance of the negative scotomas with the subsequent irregular peripheral contraction, with remaining star-like sectors, of the rapidly lessening visual fields; the progressive types of exterior and interior ocular pareses and palsies, which were always more marked in the groups of the left side; the occurrence of trophic disturbances in the corneal membrane of the left eye (the eye which was always the one which was the more greatly involved); the

enormous lengthening of the fibres of Müller—especially in the nuclear layers of the retina—giving rise to irregular elevations on the outer surface of the retina, and the gross hyperæmia and moderate degree of inflammatory infiltration of the chorioid.

A CASE OF FIBROADENOMA OF THE TRACHEA:

WITH REMARKS ON TUMORS OF THE TRACHEAL IN GENERAL.

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AND

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Tumors of the trachea are exceedingly rare. Among 3120 tumors of the upper respiratory tract seen by Moritz Schmidt (1903) there were 7 tracheal new-growths. This is less than 1 per cent. of their frequency in the larynx. This is due to the passive role played by the trachea as compared with the larynx. The lack of susceptibility of the trachea is strikingly shown by Schroetter's statistics. Among 3639 cases of disease of the upper respiratory organs, there were only 26 cases of pure catarrh of the trachea. The description of these growths is usually dismissed in a few words in the text-books. Owing to their almost certain fatality if not recognized and removed, the report of a case is not only of unusual interest, but also serves to keep the subject fresh in our mind.

The following will consist of a report of our case and a review of the literature on new-growths of the trachea. We wish to thank Dr. Mackenzie for his permission to report the case and for his supervision of our work. Our thanks are also extended to Dr. C. W. Potter for his beautiful photomicrographs illustrating the microscopic specimens.

History of Case. Mrs. J. L., aged twenty-three years, white. Was admitted to the Johns Hopkins Hospital February 2, 1903, complaining of difficulty in breathing.

Family History. Negative.

Past History. Always well and strong. Before the present trouble, no cough. Married at the age of twenty-one years; has one child living aged five months. Is now pregnant, at the beginning of the third month.

Present Illness. Nine months ago the patient noticed a slight heaviness and a feeling of choking at night. She began to cough, and there was soon some expectoration. She thought there was

something wrong with the lungs or with the heart. The difficulty in breathing has gradually grown greater, and now there is a marked shortness of breath on exertion and a constant feeling of lack of air. There is no expectoration and only a slight, hacking cough.

Physical Examination. Well-nourished woman; mucous membrane slightly pale; the teeth show a lack of enamel and a slight notching of the cutting edge. The glands of the neck are not enlarged. The lungs, heart, and the abdomen are negative.

Larynx. The vocal cords and larynx are normal. A short distance below the vocal cords one sees a tumor mass, apparently about the size of a small marble, almost hemispherical, surface smooth, mucous membrane covering it very red. It almost fills up the lumen of the trachea, and does not move on respiration or on phonation.

The patient was operated on several days after admission by Professor Halsted under chloroform anæsthesia. A preliminary tracheotomy was first performed, and then the trachea was opened above the tracheotomy wound. The growth was seen to be on the posterior wall opposite the cricoid cartilage and upper tracheal rings. At this stage of the operation the patient suddenly stopped breathing, necessitating artificial respiration. Natural respiration was established again by means of dilatation of the rectum and the growth was excised. The tracheal cannula was left in place for several days and then removed. Convalescence was uninterrupted. Dr. Mackenzie saw the patient six months later, when there was no sign of a return of the growth.

Macroscopic Description of the Tumor. The specimen is 1.5 cm. in diameter, definitely circumscribed and encapsulated. It is quite firm and elastic, with a somewhat softer area to one side. This softer area corresponds to a hemorrhagic zone. The cut surface of the tumor shows a definite capsule. On one side there is a firm tissue with a distinct fibrous network, between the meshes of which are translucent-looking areas. On pressure drops of a pure mucoid fluid are expressed, apparently from these areas. From this firm area strands and trabeculæ extend through the rest of the specimen. Between the trabeculæ are spaces of various sizes, the largest near the colloid material. Scattered through them are numerous pinpoint to pinhead size, tawny yellow, open spots.

Gross Diagnosis. Colloid adenoma. The tissue was fixed in alcohol, embedded in celloidin, and the sections were stained in hæmatoxylin and eosin, hæmatoxylin and Van Gieson's stain, and thionin.

Microscopic Description of the Tumor. The greater mass of the tumor is made up of fibrous connective tissue, which partly surrounds it as a capsule. It occurs in long, wavy masses. Intermixed with this connective tissue is a fair amount of cellular structure. The latter occurs in two forms: first as acini, secondly as cell nests without any definite arrangement. The acini are lined by a single

layer of cells, some columnar, some irregularly shaped. The nucleus of the cells is large, fairly well stained, and contains a small nucleolus. The protoplasm takes no stain and has a reticulated appearance.

The cell nests consist of round and polygonal cells between strands of connective tissue. The nuclei stain deeply, and the protoplasm is a faintly stained, homogeneous matter.

Treated with thionin, the contents of the acini take on a deep-blue stain. With Van Gieson's stain they are of a brownish color.

The fibrous tissue is present in very large amount, forming more than half of the growth. It occurs in long, wavy masses. In the section stained with thionin, numerous "mast-cells" are seen in the fibrous tissue.

The tumor is poorly supplied with bloodvessels. These consist of large blood spaces lined by a single endothelial layer.

These details are very well seen in the accompanying photographs.

The tumor is a mixture of fibrous and glandular tissue, the former predominating, and the name fibroadenoma is therefore proper.

The staining characteristics of the contents of the acini make one think of the thyroid tumors, which are described as occurring in the trachea, but the cells are certainly not thyroid gland cells and they are not arranged as in the thyroid gland tumors.

Clinically there is but little difference between new-growths of the trachea. They can be conveniently studied, however, in the following classes: 1. Neoplasms. 2. Infectious granulomata. 3. Granulations following tracheotomy and other wounds of the trachea. 4. Intratracheal thyroid growths.

1. *Neoplasms.* The following classification covers all the growths seen in the trachea:

1. Non-malignant	Papilloma. Fibroma. Lipoma. Enchondroma and chondro-osteoma. Adenoma. Lymphoma. Amyloid growths.
2. Malignant	Carcinoma. Sarcoma.

Previous to the clinical use of the laryngoscope by Türck and Czermak, growths in this region were discovered only at autopsy. Türck, in 1861, first saw a growth in the trachea in the living person. Despite the diligent use of the laryngoscope since that time, there are on record but a comparatively few cases of intratracheal tumors.

Cohen had collected, in 1889, 57 cases, all he was able to find in literature. He included in this list one case of tuberculous tumor. Lemoine, in an inaugural dissertation in 1889, added 44 new cases. As, however, 11 of these were vegetations following tracheotomy and one a syphilitic tumor, they must be excluded. Bruns, in Heymann's *Handbuch*, has made an exhaustive analysis of the literature up to

1898. He found 95 benign and 45 malignant growths, including in the latter only primary carcinoma and sarcoma of the trachea. These tumors were divided as follows: Non-malignant—fibroma, 23; papilloma, 33; lipoma, 3; chondroma and osteoma, 29; adenoma, 5; and lymphoma, 2. Malignant—carcinoma, 31; sarcoma, 14. Since that work has appeared we have been able to collect the following: papilloma, 1; chondro-osteoma, 1; carcinoma, 2; sarcoma, 8; amyloid tumors, 8; 1 case of multiple fibromyxoma of ours not yet reported, and the present reported case.

Adding these cases to those enumerated by Bruns, we have the following table, which comprises all the growths of the trachea on record:

Non-malignant	Papilloma	34	
	Chondroma and chondro-osteoma	30	
	Fibroma	23	
	Adenoma	5	
	Lipoma	3	
	Lymphoma	2	
	Fibroadenoma	1	
	Multiple fibromyxoma	1	
	Amyloid tumors	5	
		—	104
Malignant	Carcinoma	33	
	Sarcoma	22	
		—	55
			159

This makes a total of 159 tracheal tumors described up to the present date.

As in the larynx, the greater proportion of these growths belong to the papilloma and fibroma groups. They occur most frequently in the upper part of the trachea, next in the lowest part, and least frequently in the middle portion. Exceptionally they run the entire length of the trachea. They are most often found on the posterior wall.

2. *Infectious Granulomata.* In this class tuberculosis and syphilis are represented. Chronic tuberculosis gives rise to subepithelial cellular infiltrations, which break down and form ulcers of various sizes. They may extend deep, laying bare the rings, and by perichondritis destroy them. Only two instances of tuberculous tumor have been described.

Author.	How found.	Location.	Treatment.	Reference.
J. N. Mackenzie.	Autopsy.	Posterior membranous wall.	.....	Archives of Medicine, 1882, p. 107.
H. von Schroetter.	Tracheal tube.	Irregular stenosis near bifurcation.	Curetted.	Deutsche med. Woch., 1901, No. 28.

In both Mackenzie's and Schroetter's cases the growths were first thought to be cancerous. In Mackenzie's case the lungs contained tuberculous cavities. In Schroetter's case there was clinically no

demonstrable lesion of the lungs, and he therefore considered it a case of primary tracheal tuberculosis. He states that he saw the patient one year later, when she had gained in weight and the tubercle bacilli had disappeared from the sputum. He also mentions a similar case in a woman aged twenty years, but does not give a report of this case.

Syphilis sometimes causes extensive destruction of tissue, and by subsequent contraction of the cicatrices causes great distortion of the trachea. The edges of the syphilitic ulcer are sometimes the seat of papillary excrescences partly covered with stratified squamous epithelium.

Author.	How discovered.	Location.	Treatment.	Reference.
Hanszel	Laryngoscope.	Gumma of upper part.	Potassium iodide.	See Bibliography.
Bayer	Laryngoscope.	Almost complete closure of the trachea.	Mixed treatment.	" "
Glechsman . . .	Laryngoscope.	.....	.....	" "

3. *Vegetations.* These are granulomatous formations. Petel considers them exhaustively in a thesis written in 1879. Lemoine includes 11 of these in his list of benign tumors of the trachea, but incorrectly, as they are composed of granulation tissue. They form pedunculated polypoid growths, rarely larger than peas. They arise one to two months after the tracheotomy wound has been closed. They acquire an epithelial investment, sometimes covered with cilia.

4. *Intratracheal Thyroid Growths.* From a careful survey of the literature found, it is seen that these growths have occurred between the fifteenth and thirty-second years of age, slightly more often in women. They usually occur in the posterior and lateral wall, reaching from under the vocal cords, as far as the fourth tracheal ring. They were discovered in seven of the eleven cases with the laryngoscope. They form rather large, irregular tumors, with broad bases, firmly attached to the underlying structures. They consist of typical thyroid tissue, and in some the connective tissue is more abundant than in the normal thyroid structure.

Two views have been advanced to explain the presence of these growths in the trachea.

The first may be called the embryonal theory. According to this, they represent embryonic rudiments of the thyroid gland, which have been misplaced and begin to increase in size from the time of puberty. This view is taken by Heise, Radestock, Roth and Bruns. In favor of it is the location of the growth in most of the cases on the posterior wall, and in one case in a bronchus; the presence in one case of a fine membrane between the growth and the thyroid gland; the fact that in some cases there was no enlargement of the thyroid gland, and, lastly, that it is unusual for non-malignant growths to penetrate into foreign places.

The second: Ziemssen and Paltauf ascribed them to an abnormal activity on the part of the thyroid gland cells, which grow in between the thyroid and cricoid cartilages and a weakness of the cells of the tissue between the two. Paltauf materially strengthened Ziemssen's ideas through careful histological examinations. He found in his case that the thyroid gland was intimately connected with the tracheal rings and that it had grown through and was intimately mixed with the inner growths. Baurowicz accepts this explanation and notes that later on Bruns has also done the same.

SYMPTOMS. Symptoms of these various growths are only apparent when there is a considerable grade of narrowing of the trachea. They may therefore have existed for many years without having been

FIG. 1.

Photomicrograph, Dr. C. W. Potter. × 35. Zeiss planar, 20 mm. Gives a general idea of the structure of the tumor. The relative amounts of acini, fibrous tissue, and cell nests is shown. The central open space in the centre of the photograph is due to a tear in the section.

noticed by the patient. Usually shortness of breath is the first thing to attract the patient's attention. This may suddenly lead to an attack of suffocation to which the patient succumbs, as in the cases in which pedunculated polyps have closed the opening to a main bronchus or where a similar tumor is rent away by a fit of coughing and lodged in the glottis. Nicaise thinks that sudden and fatal suffocation can be explained by a spasm of the trachea.

The voice is usually enfeebled, rarely, however, to the point of aphonia. Hoarseness may or may not be present.

In cases of malignant growths there is also pain on deglutition.

Secondary symptoms are those of diffuse bronchiectasis, catarrhal bronchitis, and atelectasis following them.

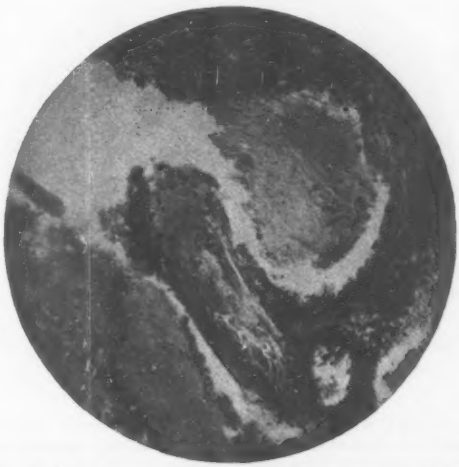
Unless relieved death occurs (*a*) by suffocation, which may be sudden or gradual; (*b*) by pneumonia, lobar or lobular; (*c*) hemorrhage from the erosion of large arteries of the neck. At autopsy there has been noted dilatation of the large bronchi, congestion of the larynx and the trachea, emphysema of the lungs and dilatation of the heart.

DIAGNOSIS. The diagnosis of tracheal growths has been rendered much simpler by the inventions of the laryngoscope and tracheoscope.

We are concerned with (1) the presence of a tracheal growth; (2) the nature of the growth.

1. As a rule, this is very easy. Progressive dyspnœa with a pure voice would lead us to suspect it after the exclusion of tumor of the

FIG. 2.



Photomicrograph, Dr. C. W. Potter. × 100. Zeiss planar, 20 mm. Acini, lined by a single layer of cells, some columnar, others irregularly shaped. The nuclei are well stained. Between the acini are strands of fibrous tissue. Section stained with hæmatoxylin and eosin.

thyroid gland and œsophagus or aneurysm of the aorta. With the laryngoscope, growths high up in the trachea, as in our case, are immediately recognized. Growths low down are much more difficult to see. However, by putting the patient in Killain's position, the lower parts of the trachea are usually very easily seen. Cases in which both these methods fail may be examined by introducing a tube directly into the trachea, after the method of Schroetter.

2. To help make a diagnosis of the nature of the tumor, we should determine the location, form, size, color, consistency, method of attachment and mobility of the growth. Even with these data it is

only rarely that a correct diagnosis of its nature is made. Papilloma, the most frequent growth, occurs usually on the anterior wall, as a pea-sized or larger growth, usually multiple, and of cauliflower-shape. It occurs at all ages. Clinically, primary tuberculous growths could not be differentiated from them. Fibroma, the next most frequent growth, occurs with equal frequency on the anterior and posterior walls, sometimes pedunculated, sometimes with broad base. It varies in size from a small berry to a walnut, is of a reddish color, and usually occurs in middle-aged persons. Adenoma or fibro-adenoma, as well as sarcoma, would be very difficult to differentiate from the last-described group. To be distinguished from the adeno-

FIG. 3

Photomicrograph, Dr. C. W. Potter. Zeiss planar, 20 mm. Ocular 3. Demonstrates the cell nests. These consist of round and polygonal cells, lying between strands of connective tissue. Several acini are also shown in this specimen. Section stained with hæmatoxylin and eosin. (Cramer's isochromatic plates used with all of these photographs.)

mata are the cystoadenomata occurring on the posterior surface of the trachea, as these originate from glands behind the muscular layer. Chondroma and chondro-osteoma appear as fine or coarse, irregular groups of nodules, scattered over the tracheal wall, usually only on the cartilaginous parts. They are very hard on palpation with the laryngeal probe. Intratracheal thyroid growths form large, irregular masses, firmly attached to the tracheal wall by a broad base. The presence of a struma of the thyroid gland will aid in making a correct diagnosis. Carcinoma forms, as a rule, a flat extensive infiltration of the mucous membrane and submucous tissues, but may occur as a circumscribed growth, or even as a single

pedunculated polyp. It occurs more frequently in men and from the ages of forty to sixty years. Symptoms develop more quickly than in the non-malignant growths.

PROGNOSIS. The prognosis is, if not operated on, most unfavorable. When operated on, the growths higher up in the trachea offer a more favorable prognosis. Of 14 benign cases reported by Lemoine as having been operated on, 10 recovered; of 12 cases not operated on, 10 died. Carcinoma is, of course, the worst form. This runs its course if untreated in from one month to two years from the onset of the symptoms. It tends, however, to remain localized, rarely perforating the trachea, and has never penetrated to the thyroid gland. Metastases to the lymph glands and organs are rare. Sarcoma of the trachea may exist for a long time. Schroetter's case was observed for twenty years.

TREATMENT. The treatment may be palliative or radical. Palliative treatment is of use in cases which are inoperable on account of the extent of the growth, as in extensive carcinoma. It consists in the use of tracheal tubes (Schroetter's or O'Dwyer's) or in tracheotomy. If the tumor is in the upper part of the trachea the ordinary tracheal cannula will suffice. If lower down a long cannula (König's or Bruns') may be used.

Radical treatment consists in excising the growth. This may be done by an endotracheal operation or by a laryngotracheotomy. The endotracheal operation may be done with the aid of the laryngeal mirror or with the tracheoscope. It is suitable for pedunculated benign growths or for benign growths with not too broad a base. They can be removed with the cold or galvanocautery snare, with forceps, or with the ring knife. The extirpation of malignant tumors by this method, as in the cases reported by Koschier, is not good surgery where a complete extirpation is possible.

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A CASE OF SUPPOSED SARCOMA OF THE CHEST WALL SYMPTOMATICALLY CURED BY MEANS OF THE X-RAY.

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THE general profession has accepted the efficacy of the *x*-ray therapy as regards external malignant conditions and certain diseases of the skin. The profession has also come to the conclusion that the *x*-rays are of no value in cases in which there is healthy tissue intervening between the growth and the impinging rays. This latter position seems to be very tenaciously held by the surgical cult. But perhaps the surgeons are excusable, inasmuch as the *x*-ray men themselves are very much divided as to the benefit to be derived in deep-seated malignant growths.

All of us who have had any experience have many failures to record. We have had many bitter disappointments, as we have seen the poor wretches sustained by a last flaring spark of hope gradually become worse as each treatment was given. Indeed, I doubt not that cases have occurred to all *x*-ray men in which the *x*-rays have seemed to stimulate the morbid process, to hasten metastasis.

Some of our good *x*-ray brethren appear to have nothing to show but enthusiasm, and others to be industriously trying to hide their light under a bushel. It seems, therefore, good and expedient, where we do have a success in deep-seated conditions, that it should be placed upon record for the encouragement of the *x*-ray fraternity, if for no other reason. Such reports ought to be in detail, so that everyone can tell at a glance just how the desired effect has been produced.

On December 27, 1902, R. F. entered my service at the Samaritan Hospital, having been referred by Drs. E. D. Ferguson and H. C. Gordinier. The patient is a schoolboy, aged sixteen years, very small for his age, white, and a native of the United States. He

complains of a prominent tumor, which evidently takes its origin from the ribs, immediately beneath and just inside of the mid-portion of the left breast. This growth is not connected with the mammary gland.

The patient's father is dead; cause unknown. His mother and one sister are living and well.

R. F. has not had any of the diseases of childhood and has always enjoyed excellent health. He first noticed this tumor in May, 1902, and it has gradually increased in size until now it is about three inches in diameter and projects from the normal line of the chest about two inches. There has not been any pain in the growth and no particular inconvenience from it. His appetite has always been good and he has not lost flesh.

During the summer of 1902 he went to the Presbyterian Hospital, New York City. I understand Dr. A. J. McCosh saw him at that time and made a diagnosis of sarcoma. Dr. McCosh refused to operate, as he did not think that it would be of any service to the lad.

The patient is of fair complexion, and, although small for his age, well built and nourished. His expression is cheerful. The pupils are equal and react to light and distance. His tongue protrudes straight, no tremor, and it is covered with a thin, white coating. Examination of the lungs, heart, and arteries is normal. The liver dulness is normal and the spleen is not palpable. Abdomen, kidneys, genital organs, mental condition, cranial nerves, electric reactions, motion, and sensation are all normal.

Upon his left chest wall is found the tumor described above. This growth is quite firm and closely attached to the ribs.

Urine, 1022, acid; no albumin. There is no note as to whether Bence Jones' albumose was looked for or not. Hæmoglobin, 92 per cent. Reds, 4,440,000; whites, 9000.

Diagnosis. Sarcoma of the left chest wall.

The following detailed line of treatment was instituted: Queen, 12-inch coil. R. Friedländer tube, which had been gradually adapted to high penetration work.

Abbreviations. = 7 in. means the length of the spark backed up at the coil terminals when the tube was in operation. D. means the distance of the nearest point on the surface of the tube from the nearest point on the surface of the patient's body. T. means the length of exposure in minutes. The face was protected by two thicknesses of T-lead tin-foil.

December 29th. = 7 in. D., 10 in. T., 10 m.

30th. Complains of headache. = 7 in. D., 10 in. T., 10 m.

31st. This morning complains of headache, and the temperature, which had been normal, went up to 101° F. = 7 in. D., 10 in. T., 10 m.

January 1, 1903. Temperature fell to 97.2° F. Patient transferred to out-patient department.

Jan. 3*d.* = 7 in. D., 5 in. T., 10 m.

6*th.* = 5 in. D., 5 in. T., 10 m. The growth now measures $4\frac{1}{2}$ inches vertically by 3 inches transversely by $1\frac{3}{4}$ inches above the general surface at its highest point. It is quite hard to the touch and is firmly attached to the ribs and has enlarged veins running over its apex.

8*th.* = 8 in. D., 8 in. T., 10 m.

10*th.* = 8 in. D., 8 in. T., 10 m.

13*th.* = 8 in. D., 5 in. T., 10 m. The boy's mother thinks that the growth is smaller and softer. The patient begins to show an undoubted cachexia.

15*th.* = 8 in. D., 8 in. T., 10 m.

17*th.* = 8 in. D., 8 in. T., 10 m.

19*th.* = 8 in. D., 8 in. T., 10 m.

22*d.* = 8 in. D., 8 in. T., 10 m. Has had la grippe. In reaction. Growth smaller.

25*th.* = 8 in. D., 8 in. T., 10 m.

March 2*d.* = 8 in. D., 8 in. T., 10 m.

4*th.* = 8 in. D., 8 in. T., 10 m. Reaction marked. Looks very cachectic.

22*d.* = 8 in. D., 8 in. T., 10 m. Growth very much smaller.

25*th.* = 8 in. D., 8 in. T., 10 m.

27*th.* = 8 in. D., 8 in. T., 10 m.

30*th.* = 8 in. D., 8 in. T., 10 m.

April 1*st.* = 8 in. D., 8 in. T., 10 m.

3*d.* = 8 in. D., 8 in. T., 10 m.

6*th.* = 8 in. D., 8 in. T., 10 m. Reaction again appearing.

20*th.* = 5 in. D., 8 in. T., 10 m.

22*d.* = 5 in. D., 8 in. T., 10 m. Growth has entirely disappeared, and the patient has a good color and says that he feels perfectly well.

24*th.* = 5 in. D., 8 in. T., 10 m.

May 1*st.* = 5 in. D., 8 in. T., 10 m.

Capitulation. 26 treatments = $7\frac{7}{26}$ in. D., $7\frac{23}{26}$ in. T., 260 m.

On March 6, 1904, nearly one year after the disappearance of the growth, I heard indirectly, through his physician, that this boy was entirely well, without the slightest evidence of the tumor.

CHRONIC INTERSTITIAL NEPHRITIS IN THE YOUNG.

By Jose L. Hirsh, A.B., M.D.,
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It is true that chronic interstitial nephritis is no longer regarded as essentially a disease of old age, yet all authorities agree that it is an extremely rare condition in the young. As the disease is in

the majority of instances associated with arteriosclerotic changes, we naturally expect to find the condition more frequent at the time of life when this alteration in the bloodvessels begins to appear. Osler[1] says, "The most common form of contracted kidney seen in this country is secondary to arteriosclerosis and seen in men over forty years who have worked hard, eaten freely, and taken alcohol in excess." Senator[3] asserts that the disease rarely begins before the thirtieth to fortieth year, and is most commonly observed in the fiftieth to sixtieth year. Flint[2] states that the disease is extremely rare in infancy and childhood, and that in an analysis of 102 cases, not a single one occurred under fourteen years of age. We find similar statements in all the text-books on the subject; still we do find some reference to it in some of the works on pediatrics.

It is not difficult to understand its rarity in childhood when we consider the chief causes leading to contraction of the kidney. Most common among them we find gout, chronic lead poisoning, alcoholism, overfeeding, chronic syphilis, and diabetes mellitus, conditions acting slowly and for the greater part associated with adult life. The relation of arteriosclerosis and kidney disease is still uncertain; either may be primary to the other; in a certain number of cases kidney disease may follow arteriosclerosis, on the other hand the arteriosclerosis may depend on the general rise of blood pressure due to the contracted kidney.

The causes cited are seldom met with in children: add to this the slow and insidious manner of the disease and its infrequency in children is readily explicable.

It is of interest to note that while in adults the proportion of cases of chronic interstitial nephritis in males to females is about $2\frac{1}{2}$ to 1 (Senator), from the number of cases which I have been able to collect in the literature I find that a larger proportion of female than male children are affected.

That this form of chronic nephritis may occur in adolescence and even in childhood has been abundantly proven by clinical observations and autopsy records. Heubner[4] collected a series of 65 cases of nephritis in childhood from his private practice and hospital records, of these 4 were of the type of contracted kidney; while none of his cases came to autopsy, the urinary examinations with the associated cardiac and vascular changes leave little doubt as to the variety of the lesions. He further states that there were but 30 cases on record in which autopsies were made.

Of Dickinson's series of 308 cases, 1 occurred between eleven and twenty years.

Ashby and Wright[5] state that 5 cases have come under their personal observations, 3 cases in girls, aged eleven, ten, and seven years respectively, and 2 cases in boys, aged five and two years; all these cases came to autopsy and the clinical diagnosis was substantiated by the post-mortem findings. Gutherie[6] collected 7

cases, between five and fourteen years, all confirmed by autopsy. Steiner and Neuretter[7] report 6 cases with autopsy. It is highly probable, however, that several of the cases of Ashby and Wright, of Gutherie and Steiner are included in Heubner's series of 30 cases.

More recently Brill and Libman[8] have reported a case of primary chronic interstitial nephritis in a girl aged fourteen years, confirmed by autopsy. This case presents several points of interest, being associated with hemorrhages into the lungs, spleen, and mesentery, general chronic arteritis, with calcified deposits in the liver and probably cerebral hemorrhage (the brain was not removed). Heubner[9] calls attention to the fact that of the cases collected by him, only 7 were primary in nature, that is, were not preceded by an acute attack of the disease; and he is of the opinion that it is almost impossible in any individual case to know if there has been a pre-existing inflammation. We are to regard those cases only as primary which develop insidiously without any evidences of previous involvement; no matter when the symptoms first show themselves they are already those pertaining to the chronic forms.

That acute inflammation of the kidneys may occur in infancy and childhood, not only following scarlet fever but many other infectious diseases, is well known.

Both Epstein[10] and Koplik[11] have shown that acute nephritis not infrequently occurs in infants as the result of gastroenteritis.

Henoch[12] was the first to note the kidney complications occasionally following varicella. Holt[13] reports several cases of acute nephritis following pneumonia. Filia[14] reports 5 cases of post-impetiginous nephritis, the infectious material gaining access through the skin to the lymphatic circulation and thence the kidney through the blood current. Perl[15] notes a case of acute nephritis following vaccination. Mettenheimer[16] notes several cases following pertussis. Freeman[17] observes the comparative frequent complication of this disease in children following influenza.

The etiological factors underlying the contraction of the kidney of childhood are often as obscure as the disease is insidious.

Weigert,[18] Baginsky,[19] Westphal,[20] and Arnold[21] have described the condition as congenital. Sutherland and Walker[22] regard congenital syphilis as playing an important role in the etiology of the disease.

Heredity seems to play a part in certain cases, as in the remarkable instance cited by Dickinson,[23] Bright's disease appearing in one family for four generations. Pel[24] records an extremely interesting family history which showed in three generations of one family 18 cases of chronic nephritis. Almost all the members of the family affected had the disease for years, but reached an advanced age and almost without exception died in uræmic coma. It is also striking that one of the children died of acute nephritis following chicken-pox, an extremely rare complication of this mild affection.

This would seem to show that this child was congenitally subject to the disease. Romme[25] likewise relates a family history showing 18 cases of nephritis in one family in three generations. In the case of Brill and Libman the three oldest children had Bright's disease.

Two cases of contracted kidney in the young have recently come under my observation, both associated with alterations in the blood-vessels, though of an entirely different nature:

CASE I.—C. W., white boy, aged fifteen years, was brought to the University Hospital on account of an uncontrollable hemorrhage from the gums following the extraction of a tooth the day previous. He complained of being short of breath and feeling very weak. He was put to bed and continuous pressure applied to the gum, which stopped the bleeding in a few hours. The following history was then obtained: The family history presents nothing of importance. As far as could be learned no other member of the family presented a history of kidney disease.

Patient had been a strong, robust child, had measles at six years, and chicken-pox at eight years, otherwise he had never been confined to bed. He attended school until his thirteenth year, after which he did light work about an office. About one year ago he began to complain of feeling very tired on slight exertion; his appetite began to fail and his sleep became restless. He noted that it was necessary to get up at night to empty his bladder, and this has continued up to the present time. Of late he has been having headache at irregular intervals, and the day previous to his entrance to the hospital he had an attack of especial severity which was associated with pain in the upper jaw and for which the tooth had been extracted. He had never had hemorrhage before and there were no bleeders in his family.

Present Condition. Patient is pale; the mucous membranes are almost colorless. The pupils are slightly irregular, but respond to light and accommodation. The neck is short and there is visible pulsations of the carotids. The chest is well formed; the lungs are normal, except a slight rale occasionally heard at the base of both lungs. The heart is rather tumultuous; the apex beat is noted most prominent in the fifth intercostal space, and just without the nipple line. The area of cardiac dulness is increased both toward the right and left; there is a soft systolic blow at the apex, and the second aortic is markedly accentuated. The radial pulse is full, of moderate tension, though compressible, but is completely cut off with some difficulty; there are 80 beats to the minute.

The liver extends one finger's breadth below the costal margin; the spleen is not palpable. There is no œdema about the extremities. Temperature, 99; respiration, 24.

Urinary examination showed the urine to be increased in quantity, though the exact amount was not noted. Color, light; specific gravity, 1012; no sugar; albumin, a very small amount by Heller's

ring test. Casts: a few hyaline and an occasional granular cast were noted. Repeated examinations during patient's stay in the hospital gave about the same results, although on several examinations albumin was absent.

Blood examination showed 3,700,000 red blood corpuscles, 6500 white. The coagulation time was not diminished.

After rest in bed for a few days, patient's condition seemed to improve; however, after being about the wards for a week there was noted beginning œdema about the ankles, this gradually increased though at no time was it sufficient to cause any inconvenience. Dyspnœa became more marked and patient died five weeks after entering hospital.

Autopsy, Four Hours after Death. Body length 120 cm. Muscles flabby, skeletal development good. Rigor mortis absent. Œdema of the lower extremities. Both pleural cavities contain about 200 c.c. of a straw-colored fluid. The lungs are congested and on pressure a large amount of frothy serum exudes from the cut surface. The heart is markedly enlarged; this is chiefly due to hypertrophy of the left ventricle, which measures 2 cm. in thickness; the right ventricle measures 9 mm. The valves show no decided changes; both coronaries are somewhat thicker than normal. Weight of heart 300 grams.

The left kidney is smaller than normal; it weighs 68 grams; size 8 x 4 x 2 cm. The capsule is adherent, and when removed the outer surface of the cortex is seen to be granular; cysts are scattered over the surface. The substance of the kidney is firm, the cortex is reduced in size, and the entire section has a clouded appearance. The right kidney presents the same general appearance; weighs 80 grams; size, 8 x 6 x 3 cm.

The liver shows evidences of passive congestion; weighs 1200 grams. The gastrointestinal tract shows a few punctate hemorrhages throughout the mucosa. Spleen and pancreas normal.

The aorta is decidedly atheromatous; there are several calcareous plates in the dorsal and lumbar regions, spots of fatty degeneration are present throughout its whole extent.

Anatomical Diagnosis. Chronic passive congestion of the lungs and liver; hypertrophy of the heart; chronic interstitial nephritis; arteriosclerosis of the aorta.

Microscopic examination of the kidneys shows a great increase of the interstitial connective tissue; many of the glomeruli are shrunken and the capsule of Bowman thickened; some of the glomeruli are completely replaced by fibrous tissue; the cells of the tubules are degenerated, and the walls of the bloodvessels are much thickened. The sections show an advanced stage of contracted kidney.

The chief point of interest in this case besides the marked interstitial nephritis is the marked arteriosclerosis of the aorta. Sim-

nitzky[26] has made a careful study of arteriosclerosis in young individuals, and in a recent communication presents a series of 38 cases varying in age from four to twenty-four years. He states that he has found the condition present to some extent in 27.5 per cent. of all cases up to the twenty-fifth year. He believes the infectious diseases play an important role in the etiology of the disease.

Ballantyne[27] found decided atheromatous changes in the aorta and pulmonary arteries in an eight months' fœtus. Marfan[28] describes similar lesions in three boys, aged nine, twelve, and thirteen years respectively. Sanne[29] mentions a case of arteritis chronica in a child aged two years, and an aortic aneurysm in a boy aged thirteen years.

The influence of heredity must not be lost sight of in these cases. Just as contracted kidney may be found in one family for several generations, so may changes in the bloodvessels. Osler speaks of this as "a tendency which cannot be explained in any other way than that in the make-up of the machine bad material was used for the tubing."

CASE II.—L. B., white, unmarried female, aged eighteen years, entered the University Hospital on July 12, 1903, complaining of inability to control her bladder and frequent micturition. The family history is bad. Her maternal grandmother, mother, and two maternal aunts died of cancer of the breast. Her father suffered with some stomach trouble for eighteen months prior to his death. Brothers and sisters are healthy, although one sister, aged twenty-three years, has never menstruated. There is no history of tuberculosis or kidney disease.

Patient was never a very strong child; has had measles, pertussis, and diphtheria. Began menstruating at ten years and has continued normal since. When fourteen years old patient fell from a tree, injured her back, and was unable to move about for one year; she has suffered now and then from this trouble to the present time. She says that her "kidney trouble" began two years ago.

Patient is anæmic, her general development corresponds to a girl of about fourteen years; breasts are but slightly developed. Pupils are regular and respond to light and accommodation. Diffused moist rales are present over both lungs. Area of cardiac dulness is increased, the apex beat is 1 cm. without the mammary line; no murmurs are to be heard, but the second aortic sound is accentuated. Abdominal organs are negative. Tension of radial pulse is not increased, soft and easily compressible, no evidences of sclerosis. Beats 80.

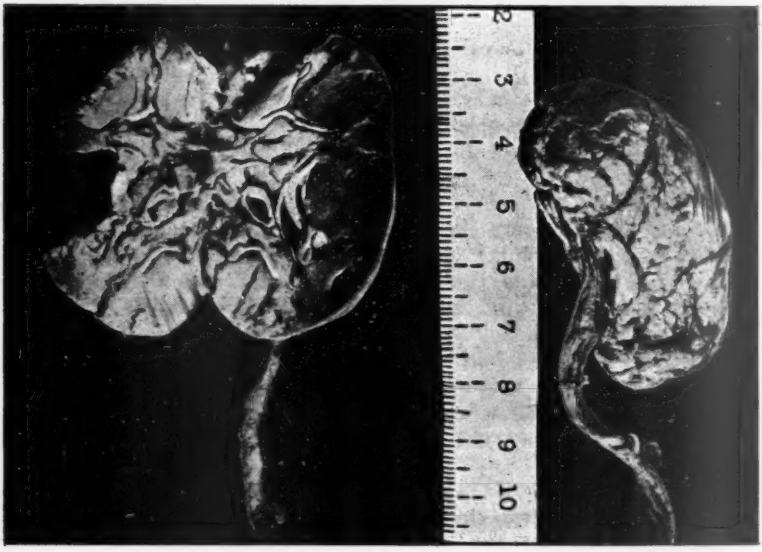
Ophthalmological examination is negative.

Urine is increased in quantity; specific gravity, 1010; light color; no sugar; small amount of albumin; few hyaline casts; some pus cells. In the lower dorsal region there is a protrusion of the spinal

process, which is painful on pressure, and is probably an old Pott's disease. There is some anasarca of lower extremities. Patient's condition continued unaltered until July 25th, when she began to complain of headache, she gradually became dull, and two days later comatose, and died July 28th.

Autopsy, Twelve Hours after Death. Body length 175 cm. Very slight build. Skeletal development small, muscular development good. Rigor mortis well marked. The tenth and eleventh dorsal vertebræ are protuberant, and the skin over same is excoriated.

The heart is slightly enlarged; there is no abnormality about the valves; the wall of the left ventricle is hypertrophied, measures



Kidneys in Case II. Actual size.

15 mm. in thickness; wall of right ventricle measures 7 mm. in thickness. Weight of heart 175 grams. The lungs are somewhat small, dark in color, much congested and crepitate throughout; there are no evidences of tubercle. The spleen and liver are somewhat smaller than normal, though normal in appearance. The gastrointestinal tract is normal.

The kidneys are extremely small. The right kidney measures 5 x 2.5 x 2 cm. and weighs 18 grams.; the left kidney measures 4.5 x 3 x 1.5 cm. and weighs 22 grams. Capsules of both kidneys are slightly adherent, and the cortex granular. On section the cortex is narrow, very firm and of a light color; there is no definite

boundary line between the cortex and medulla; the pyramids are likewise contracted and have the appearance of scarred tissue.

The uterus appears somewhat smaller than normal; length 5½ cm., width at fundus 4 cm. The ovaries are well developed and show several false corpora lutea. Bladder normal.

The aorta is abnormally small; at its origin it measures 4.8 cm. in diameter; just below the diaphragm it measures 3.5 cm. in diameter. Throughout its entire extent it admits the small finger with some difficulty. There are no evidences of atheroma.

Both the renal arteries are small.

Examination of the inner surface of the 10th and 11th vertebræ shows a calcareous mass between them, an old tuberculous lesion.

Anatomical Diagnosis. Hypertrophy of the heart; congestion of the lungs; chronic interstitial nephritis; healed Pott's disease; congenital narrowness of the aorta and renal arteries.

Microscopic examination of all the organs with the exception of the kidneys exhibit nothing of especial interest. The alterations in the kidneys affect all the elements, the glomeruli, the tubules, the interstitial connective tissue and the bloodvessels. Many of the glomeruli are shrunken, some appear as a hyaline ball, the capsule of Bowman is thickened; other glomeruli are hypertrophied and congested. Scattered throughout the cortex in areas is seen a small-cell infiltration. In many parts the tubes are diminished in size or completely obliterated; in others they are dilated and filled with degenerated epithelial products. The intertubular connective tissue is thickened throughout, giving the medulla in places a fibroid appearance. The walls of the smaller bloodvessels are much thickened.

It may prove of interest to call attention to the size and weight of some of the reported cases of contracted kidney in the young.

No.	Author.	Age.	Sex.	Weight.	Size.	Combined weight of kidneys.
1	Barlow	6 years	F.	R. 13 grm. L. 21 "	5 × 4 × 0.5 cm. 6 × 3 × 1.5 "	33 grm.
2	Ashby and Wright . .	11 "	F.	R. 75 " L. 24 "	Not stated. " "	99 "
3	Ashby and Wright . .	12 "	M.	R. 38 " L. 37 "	" " " "	75 "
4	Bull	13 "	F.	R. 35 " L. 20 "	7.5 × 4 cm. 5 × 3 "	55 "
5	Hanford	13 "	F.	R. 60 " L. 15 "	8½ × 4½ × 2 cm. 5 × 4 × 2 "	75 "
6	Brill and Libman . .	14 "	F.	R. 59 " L. 34.5 "	9 × 4 × 3 cm. 6 × 3.5 × 2.5 cm.	93.5 "
7	Hirsh	18 "	F.	R. 22 " L. 18 "	5 × 2½ × 2 cm. 4½ × 3 × 1.5 cm.	40 "
8	Weigert	6 weeks	...	R. ..... L.	1.7×1.0×0.5 cm. 2.0×1.1×0.4 "	Congenital.

The relationship between congenital narrowness of the aorta and arterial system and primary atrophy of the kidney has been noted by Lancereaux,[30] and by Besancon and Poillon.[31]

Bizot gives the average diameter of the aorta at its origin as 7 cm. in males and 6.4 cm. in females. Beneke gives the average in youth as 6 cm. The authors mentioned found in the narrow aortas a circumference of 4.2 to 5.2 cm.

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KERNIG'S SIGN:

WITH REPORT OF CASES WHERE THE ANGLE HAS BEEN ACCURATELY DETERMINED.

By Joseph L. Miller, M.D.,

of Chicago.

Kernig, on September 21, 1882, read a paper before the St. Petersburg Medical Society on the presence of a sign which he considered pathognomonic for meningitis and which has since been known as Kernig's sign. This sign consists in inability to extend

the leg fully when the thigh is at right angles to the trunk. Kernig made the test by having the patient sit on the edge of the bed with legs overhanging and then attempting to extend the legs. Osler first called attention to the fact that the sign could be elicited by having the patient lie on his back, and then, after flexing the thigh on the trunk to a right angle, an attempt is made to extend the leg on the thigh. This is a more satisfactory position, as it enables us to determine the angle with greater ease, and even very sick patients are not inconvenienced. Rudolph recommended making the test by first fully extending the leg, then flexing the thigh on the pelvis and measuring the angle at the hip, as by doing this only one angle need be gauged, while in the original method the thigh must first be placed at right angles to the trunk and then extend the leg. This I believe is an unnecessary refinement, as it is not essential that the angle of the thigh to the trunk be exactly a right angle, but approximately so, a point which can be sufficiently gauged by the eye; and, second, on account of the more irregular contour of the parts at the hip, it is more difficult to measure the angle with an instrument than it is at the knee. In the normal individual the leg can be almost completely extended when the thigh is at right angles to the trunk. Kernig reported that in case the sign was positive, the angle was about 135 degrees, but might reach 90 degrees, and since then the generally accepted view has been that an angle of 135 degrees or less is a positive Kernig. He called especial attention to the fact that in a patient with positive signs the leg could be completely extended, if the precaution was not taken to place the thigh at approximately a right angle to the trunk. He also reported that the sign might be present in the arms. He considered that this was an early and constant sign in meningitis, often persisting until the patient was well along in convalescence. His conclusions were based upon the examination of 15 cases of meningitis, the diagnosis being confirmed in 8 by autopsy. Thirteen of these cases were of the cerebrospinal form, 1 tubercular, and 1 suppurative. He also obtained the sign in spinal caries, pachymeningitis hemorrhagica, localized meningitis from otitis media, 1 case of hyperæmia of the meninges which he reports was possibly a beginning tuberculosis, chronic leptomeningitis, and a slight Kernig in a case of œdema of the pia.

Kernig's paper did not excite much attention. The first published confirmation of his results was made by Friis, in 1887, and again in 1892. Since then numerous reports have been made. All of these have emphasized the diagnostic value of the sign, and yet many of the recent works on medicine, neurology, or diagnosis fail to mention the sign; others merely refer to it without commenting on its value. None of these works report the various conditions, besides meningitis, where the sign is present or give accurate information as to what degree of flexor contraction constitutes the sign.

The lack of general knowledge of the subject is due, in part, to its unreliability. However, we have comparatively few signs which can be looked upon as pathognomonic, and lack of constancy merely lessens the value of the test, provided we are familiar with the source of error, and thus give it the proper weight.

Herrick reported 19 cases of meningitis: 9 cerebrospinal, 2 pneumococcus, 7 tubercular, 1 syphilitic. In 2 cases, 1 probably tubercular, the other following a pneumonia and associated with otitis media, the sign failed. Both of these cases were children, aged three and four years respectively, and the test was only made shortly before death, which may account for the result, as it has been noted that the rigidity of the neck may disappear or be much lessened just before death. In 1 case of probable tubercular meningitis, it was present in one leg, but not in a typical manner in the other. He examined 25 healthy individuals, in all of whom the sign was absent. In 100 cases of various troubles, the Kernig was present in only 2, 1 a gonorrhœal rheumatism of the knee, the patient having remained in bed with the legs flexed for several weeks, the other a subdural hemorrhage.

Netter has published two series of cases of meningitis, in all 72 in number, with positive Kernig in 91 per cent. In 1 of the negative cases the child had an advanced tuberculosis, in another the test was made only once.

Friis, of Copenhagen, in 1887, reported it present in 53 out of 60 cases. In 2 of the negative cases the test was doubtful, in 3 the examination could not be properly made, and in 2 it was absent.

In a later series in 1892, all of which were of the epidemic type, it was present in 21 out of 26 cases. He considered that there was no relation between the sign and the rigidity of the neck.

Bull found the sign present in a case of tuberculous meningitis, in a solitary tubercle of the cerebellum, with a few miliary tubercles in the overlying pia, and in a case of otitis media, with thrombosis of the transverse sinus and basal ecchymosis.

Blumm reports it present in 7 out of 9 cases of cerebrospinal meningitis.

Thyne, in a case with hemorrhage into the right lateral lobe of the cerebellum and the fourth ventricle.

Packard reported several negative cases: 1, a child, aged sixteen months, with general miliary tuberculosis, the membranes of brain and cord being involved, where daily examination gave negative results. In a second case of leptomeningitis following pneumonia, the sign was always absent. In a third case with miliary tubercles over the motor area of the cortex, repeated examinations were negative. He did not attach much importance to the sign in infants.

Magri refers to cases where, in uncomplicated typhoid and pneu-

monia, the sign was present, and to a case of his own where the patient had sciatica.

Sailer found the sign present in a case of focal encephalitis of the ascending parietal lobe with the overlying meninges congested, and in a patient where the diagnosis of unilateral lesion of the medulla was made.

Clark, in 2 cases of tubercular meningitis, never found the angle less than 150 degrees, and the sign was absent in a case of acute cerebrospinal meningitis of undetermined bacterial nature, where there was marked exudate over the thoracic cord.

Rudolph, by means of an instrument, measured the angle in 162 cases, found it less than 180 degrees in 60 per cent. of cases; 165 degrees or less in 0.4 per cent.; 135 degrees or less in 6 per cent. As above mentioned, his method was to measure the angle at the hip. Shields measured the angle in 100 cases, both febrile and afebrile, and in 5 found an angle of 120 degrees or less. Two of these were typhoid; in 1 unilateral, 100 degrees; the other bilateral, 110 degrees. In the former it did not disappear during convalescence. One case of uræmia, angle 110 degrees. The other 2 were hemiplegics, with angles of 115 degrees and 120 degrees respectively.

My own observations were confined chiefly: first, to acute infections—mainly typhoid and pneumonia; second, various forms of meningitis; third, central and peripheral nervous troubles; fourth, patients who had been confined to bed for several weeks, chiefly convalescents from acute infections and surgical cases. The material was obtained from the Cook County Hospital. The angle was measured by means of an inclinometer, an instrument of accuracy. On account of the irregular contour of the parts, it is, of course, impossible to obtain very exact measurements, even with an accurate instrument. All the tests were made with the patient in the dorsal position. The thigh was first placed at right angles to the trunk, then the leg was extended on the thigh until it either caused pain or could not be farther extended without using considerable force. Babinski's reflex was observed in most of the cases, and the results of this test are placed in the table.

In none of the cases examined was there an angle of 180 degrees, and in several healthy individuals it was impossible to obtain this angle without either allowing the thigh to recede from its position at right angles to the trunk, or using sufficient force to cause discomfort, the average angle being about 165 degrees.

An angle of 115 degrees or less has been considered a positive Kernig. This I believe is better than 135 degrees, as suggested by Kernig, as it excludes very few cases of meningitis, and an angle of 135 degrees is not infrequent in other conditions. A bilateral test was made in all cases. In the following table are summaries of the results:

Disease.	Total cases.	Kernig presents 115° or less.	Angle 120°.	Angle 125°.
Typhoid	48	4	5	9
Transverse myelitis	4	1		
Hemiplegia	17	7	2	2
Syphilitic spastic paraplegia	7	4	1	
Primary spastic paraplegia	1	1		
Carcinoma of spine	1	1		
Infantile paralysis	1	1		
Multiple neuritis	16	3	3	3
Sciatica	12	2	1	1
Delirium tremens	3	1		
Hysteria	3	...	...	1
Tetany	1	1		
Uræmia	2	2		
Illuminating-gas poisoning	1	1		
Cerebrospinal meningitis	6	4	1	
Tuberculous meningitis	3	3		
Diplococcus pneumoniæ meningitis	1			
Cerebrospinal syphilis	4	3		
Thigh fracture	3	1	1	
Pneumonia	22	3	...	5
Locomotor ataxia	6	1		
Lumbago	1			
Pericarditis	1			
Tetanus	1			
Status epilepticus	1			
Chronic chorea	1			
Acromegaly	1			
Paralysis agitans	4			
Syringomyelia	1			
Multiple sclerosis	2			
Typhoid spondylitis	1	...	...	1
Landry's paralysis	1			
Trichinosis	2	...	1	
Gonorrhœal myalgia	2			
Progressive muscular atrophy	1			
Amyotrophic lateral sclerosis	1			
Brain abscess	1	...	1	
Surgical cases exclusive of thigh fractures	8			

A Kernig was present in 45 of the 190 cases. Four of the 10 cases of meningitis failed to give the reaction, although 1 of these had an angle of 120 degrees. This was an epidemic cerebrospinal. One epidemic cerebrospinal had an angle of 150 degrees in the second week. The other negative cases were 1 each of pneumococcus and tuberculous meningitis, the latter giving an angle of 125 degrees. Strictly speaking, in only 2 cases of meningitis was there an absolute absence of the Kernig sign. In 1 of the cases the sign only appeared late, several days after a lumbar puncture, demonstrating the specific micro-organism. The diagnosis in all of these cases was verified either by lumbar puncture or autopsy.

Positive results were obtained in 7 of the 17 hemiplegias, and 4 others had an angle of 125 degrees or less. The sign was bilateral in 4 cases. One of these proved to be a hemorrhage into the ventricle. One was a double hemiplegia, with an interval of several weeks between the attacks. The other 2 were apparently uncomplicated hemiplegias, with no especial evidence indicating a ventricular or basal meningeal process.

Seven cases of Erb's syphilitic spastic paraplegia were examined: 4 gave the Kernig bilaterally, 1 had an angle of 120 degrees, the

other 2 were completely negative. A case of primary spastic paraplegia was positive.

Of interest is the positive test in 3 of 16 cases of multiple neuritis, and 3 cases with an angle of 120 degrees, and 3 with an angle of 125 degrees. The sign was bilateral in all the cases. The majority of the cases examined were of several weeks' standing; 1 of the positive was of two months' duration, another one week. Only 3 cases of this series had an angle greater than 145 degrees.

Twelve sciaticas were examined, with 2 positive results. One of the negative cases had an angle of 125 degrees; another 120 degrees. The positive cases were both of a severe type. The patient with an angle of 125 degrees had a very mild attack.

Several have reported the sign present in uræmia. Only 2 cases were examined for the sign, and both were positive; 1 bilateral, the other unilateral.

Three out of 4 cases of cerebrospinal syphilis gave a bilateral positive test, the other was completely negative.

With a view of ascertaining whether the sign might develop in patients who had been confined to their bed for several weeks, the uninjured extremity in 3 cases of thigh fracture was examined, with 1 positive result and 1 with an angle of 120 degrees. Two patients who had been in bed for three weeks following a herniotomy were negative. Two patients in bed for four and six weeks, respectively, with fractured ribs were negative.

The pneumonias examined were the severe cases that entered the hospital. In all 22 cases were tested. Three gave a positive Kernig, 5 gave an angle of 125 degrees, and the remainder were negative. In those who gave the test there were no signs or symptoms of meningitis. The typhoids examined included those in the active stage of the disease and convalescents—the latter for the purpose of determining whether a prolonged stay in bed was a causative factor in the sign. In all 48 cases were examined: 4 were positive, 5 had an angle of 120 degrees, 9 an angle of 125 degrees. Twenty-four were in the active stage of the disease, 19 of these at least moderately severe cases. None of these gave a Kernig, all of the positive cases being in the convalescents. Those giving an angle of 120 degrees, 5 in number; 3 were in the active stage of the disease, 5 convalescents. Those giving an angle of 125 degrees, 5 were in the active stage of the disease, 4 convalescents. Only 1 of the convalescents had lain in bed with the knees drawn up.

Two cases of trichinosis were examined. In both of these the diagnosis was confirmed by finding the unencapsulated parasite in a piece of excised muscle and by the presence of an eosinophilia. One patient was in the very acute stage with intense muscular rigidity and soreness, sufficient, at least, to suggest a meningeal process, and the angle was 120 degrees. The other patient was in early convalescence, and the sign was negative.

The patient with the illuminating-gas poisoning died, and, as an autopsy was not obtained, it would be impossible to exclude a chronic cord or cerebral lesion which might have been responsible for the sign.

The results of these tests agree quite well with the investigations of others, and Henoch was first to call attention to the unreliability of the sign. Its frequency in other conditions, some of which may resemble meningitis, as an illustration, trichinosis and uræmia, lessen its diagnostic value. Its not infrequent absence in meningitis, especially in the tubercular form, and its often late and transitory appearance, lessens its significance. On account of its late or transitory appearance, daily or at least repeated examinations should be made. The presence or degree of sign is no index of the severity of the symptoms or gravity of the case.

Several theories have been advanced to explain the cause of the Kernig phenomena.

Netter considered that on account of inflammation the roots of the spinal nerves were irritated, and in extending the leg on the thigh the sacral nerves are stretched, causing reflex contraction of the flexors.

Friis suggested it was due to irritation of the cauda equina by the infected cerebrospinal fluid.

Chauffard considered it an exaggerated normal phenomena due to hypertonicity of the muscle.

Sailer would explain the sign by an irritative lesion of the pyramidal tract that diminishes but does not destroy its functional activity.

Rudolph believes the increased muscular tone, probably due to cerebellar irritation, is responsible for the sign in meningitis, and that recumbency may be the cause in some cases.

Several have explained the phenomena by increased intracerebral pressure, but Roglet's experiments show that in animals increased intracerebral pressure does not cause a muscular contraction of this nature. Rudolph reports slight decrease in the Kernig after spinal puncture.

From a clinical standpoint, it would appear that the various disease conditions in which the sign may be found excludes the probability of a common origin. Netter's view of nerve irritation might explain its frequency in meningitis, neuritis, and sciatica. Pyramidal-tract involvement offers the most plausible explanation of its presence in hemiplegia and spastic paraplegia.

Babinski's reflex was examined in most cases, in quite a number of patients contractions either negative or positive could not be obtained. In those who gave a positive reaction, repeated tests were made in order to be certain the reaction was not accidental, and any case that showed a single plantar flexion was classed as negative. In 17 cases of hemiplegia 11 gave a positive reaction, 5 negative,

and 1 not tested. A case of illuminating-gas poisoning gave a typical positive reflex. As the patient died, we were unable to exclude a possible pre-existing cord lesion. Two typhoids gave the reflex; it differed, however, from the cases with lateral tract involvement by being slow and of very moderate degree, but always getting a dorsum flexion; neither of these cases had any other signs of involvement of the lateral tract. One of 4 cases of cerebrospinal syphilis was positive, and it is not improbable that the substance of the cord was involved. One case of gonorrhœal myalgia gave a slight positive reaction. A case of progressive muscular atrophy without any other signs of lateral-tract involvement gave the test in a very typical manner. The reaction was characteristic in a case of amyotrophic lateral sclerosis. One of 4 cases of transverse myelitis gave a positive test, and 1 case of carcinoma of spine. Seven of the 8 cases of spastic paraplegia were positive.

SUMMARY. 1. A maximum angle of 115 degrees gives more valuable results than does an angle of 135 degrees, as proposed by Kernig.

2. The angle obtained in any individual case depends, in part, upon the force used in extending the leg, and for this reason actual measuring of the angle is not essential.

3. The sign is present in a large percentage of the cases of meningitis; it is, however, not constant, may be transitory, or only appear late; therefore, daily examination should be made for its presence.

4. It is present in a typical manner, occasionally in a number of widely different disease conditions, and for this reason it is probable that there is not a uniform cause for the sign.

5. The sign is occasionally unilateral, exclusive of cases of hemiplegia or local trouble, which might explain its unilateral presence.

6. The presence of the sign in cases of suspected meningitis is merely another factor favoring the diagnosis. Its absence, especially early, is not infrequent, and should not be allowed to outweigh the positive findings.

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REPORT OF TWO CASES OF VOLVULUS OF THE ENTIRE MESENTERY.[1]

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The privilege of reporting the following case has been granted me by Dr. John B. Deaver. P. K., male, aged five years, was admitted to the Mary J. Drexel Home with a history of having been sick for five days, during which time he had suffered with nausea and vomiting and inability to expel flatus or fecal matter. When admitted he was shocked, being very weak, with cold, clammy skin and a rapid, running pulse. The abdomen was markedly distended. Rectal enemata were retained, being recovered through a rectal tube, not discolored. The patient did not react under treatment and died twelve hours after admission.

Partial post-mortem examination revealed the following: Peritoneal effusion of a serosanguineous character was present in large amount. The omentum was small, irregular in shape, and contained a small amount of fat. There were no peritoneal adhesions and no inflammatory exudate. The stomach was normal in size, but was pushed upward by the distended small bowel. The duodenum was normal, but slightly congested. The remainder of the small bowel was markedly distended and of a dusky hue. The bowel was drawn out of the abdomen when it was discovered that the root of the mesentery was so twisted on itself that it appeared like a cord. The turns of the mesentery were from right to left. The number of turns was not noted. By lifting the small bowel *en masse* the mesentery was readily untwisted.

The doctor who made the necropsy became infected during the examination, the infection being so virulent that, in spite of most active treatment, he suffered from general septicæmia, from which it was feared he could not recover. This unfortunate termination was, however, happily replaced by a perfect recovery after a tedious illness.

The second case was C. B., male, aged thirty-four years. He had had an attack of acute appendicitis in October, 1902, for which he was operated on in the German Hospital. The appendix was gangrenous; the intestine was injected, inflated, and covered with lymph. There was a local collection of pus at the base of the appendix. The abdominal cavity was cleansed as thoroughly as possible, after removal of the appendix, and four pieces of gauze were inserted for drainage, no attempt being made to close the wound. A fecal fistula developed which closed without operative interference before the patient left the hospital. After his discharge the patient suffered from intermittent pains in the right iliac

[1] Read before the Philadelphia Academy of Surgery.

fossa and along the line of the cicatrix. He was examined on May 2, 1903, at which time he complained of constipation, loss of appetite, and dull pain in the right iliac fossa. The scar was firm, the abdomen soft, with no points of tenderness. At 5 P.M., May 29, 1903, while walking up stairs, the patient was suddenly doubled up with most severe pain at the site of the cicatrix. He was nauseated, but did not vomit. He had had a bowel movement in the morning, but from the time of the onset of the violent pain until after a subsequent operation he was unable to pass either flatus or fecal matter. He was admitted to the German Hospital about 8 P.M. of the same day, at which time I saw him. He was in great distress, with severe cramp-like pains over the entire abdomen, but most marked in the right iliac fossa. The abdomen, which was slightly distended, was very tender. The rectus muscles were rigid. There was a large hernial opening at the site of the cicatrix which had not been present one week before. The temperature was 97.2°, pulse 58, respirations 26. I made a diagnosis of acute intestinal obstruction and advised immediate operation, to which consent was given.

Operation about 9 P.M., four hours after the onset of pain. Under ether anæsthesia an elliptical incision was made around the cicatrix, and the peritoneum was opened to the inner side of the cæcum. In dissecting the latter from the anterior abdominal wall, to which it was firmly adherent, it was unintentionally opened but immediately closed with two rows of Lembert sutures. Inspection showed the intestine near the ileocæcal junction to be bound together by dense adhesions, some of which were as large as the little finger. There was partial obstruction at the ileocæcal junction. With the exception of the last portion of the ileum and the duodenum, the entire small intestine was partially collapsed, lustreless, dusky red in color, and of a doughy feel. All adhesions were separated, the denuded surfaces being covered with cargile. The small intestine was drawn out of the wound in a search for the cause of the peculiar condition of the gut, when it was found that the entire mesentery was twisted upon itself, about a three-quarter turn, from left to right. The bowel was lifted up in a towel and the entire mass turned from right to left. This relieved the twist in the mesentery and returned it to its normal position. The circulation of the bowel was immediately re-established, the normal color and lustre rapidly returning. The separate layers of the abdominal wall were dissected out and the wound closed with tier sutures of silk; 500 c.c. of salt solution were injected into the rectum before the patient left the operating table. He reacted well. Flatus was passed through a rectal tube six hours after the operation, and voluntarily six hours later. The bowels moved freely on the second day. With the exception of slight infection in the lower part of the wound, the patient had no unfavorable symptoms and was discharged from the hospital on the 17th day after operation.

These two cases demonstrate the value of early operative interference in cases of suspected intestinal obstruction. The first case was brought to the surgeon when the patient was practically moribund, and of course no relief could be afforded. It is probable that the perfect recovery made by the second patient was largely due to the short interval which elapsed between the onset of the acute symptoms and the time of operation. The second case also shows the value of thorough inspection of the abdomen in cases of obstruction. I expected to find nothing but an occlusion of the bowel due to adhesions or bands. Had the real cause of the trouble been overlooked, the patient would necessarily have died.

In a very interesting article published in THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES for May, 1903, Dr. George Tully Vaughan cites twenty-one cases of volvulus of the entire mesentery. Seventeen of these were operated, with four recoveries, a mortality of about 76 per cent. This mortality, as stated by Dr. Vaughan, is due to three causes: First, the serious nature of "a condition which strangulates almost the entire small intestine, injures the sympathetic plexus, and perhaps produces a rapidly fatal toxæmia." Second, the delay in operating. Third, "the difficulty in recognizing the true condition in order to act intelligently, four of the operators cited confessing their inability to do so after opening the abdomen. The patients died without relief, the true condition being at last disclosed at the necropsy."

A SIMPLE METHOD FOR THE REDUCTION OF LUXATIONS OF THE HUMERUS.

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THOUGH the range of motion through movement of the humerus is great, the scapula normally admits of but little motion when the humerus is held in a fixed position. In luxations of the joint, however, the range of passive scapular motion is considerable, and it has been through studies of the possibilities due to this fact that the following methods have been evolved. They are, of course, susceptible to various modifications, according to the dexterity of the surgeon. The studies have extended over a period of four years' time, and include fifteen cases of the author's and nine cases which were referred to her; this number comprising only such cases as were uncomplicated by fracture of the scapula or clavicle, or of the necks of the humerus.

I. This method is applicable to subspinous dislocations, as well as to downward and forward luxations.

The surgeon stands behind the patient, who may sit or stand, as is convenient. In performing the manipulations the writer uses the hand corresponding to the side upon which the lesion exists.

The hand of the operator is partially closed, the thumb extended, and the wrist pronated. The ball of the thumb is placed below, against, and parallel to the lower margin of the scapula on the axillary border, just external to the inferior angle.

Firm pressure is exerted, and the wrist is slowly and steadily supinated, pressure upward and inward being exerted at the same time. This manipulation, if properly performed, pushes the lower angle of the scapula upward and toward the median line, depressing the lower lip of the glenoid cavity, and usually results in the prompt reduction of any variety of humeral dislocation.

In the subspinous variety, should reduction not occur, and a repetition of the manipulations bring no better result, pressure with the other thumb upon the head of the dislocated humerus, in the direction of the long axis of the bone, should be added, inserting the digit as deeply upon the head as is possible.

II. In subcoracoid or subglenoid dislocations, the operator stands behind the patient, as before, and places his hands on the patient's shoulders, with the palm of the hand at the base of the ring finger resting upon the acromion process of the scapula, the ball of the finger being placed below the clavicle. The ball of the middle finger is placed just above the clavicle, and that of the thumb beneath the spine of the scapula as far toward the inner end of the spine as is compatible with stability of position. The fingers should be slightly flexed, but not enough so as to interfere with firm pressure on the acromion process, nor so much so as to substitute the tips for the balls of the digits. The elbows should be extended. Quick but steady pressure should then be exerted in a downward, inward, and backward direction, considerable force being used.

This method has proven prompt and efficacious, even in cases in which the parts were greatly swollen from contusions sustained at the time of injury.

The following advantages are claimed for both methods:

1. There is little risk of further damage, since a short lever is used instead of a long one.

2. In cases in which fractures of the humerus, or of the bones of the forearm are present, the surgeon is enabled to effect reduction in a manner which does not necessitate the handling of the limb.

3. The patient does not suffer any great amount of pain during the procedure.

4. The patient is apt to be docile, since he does not expect reduction to be effected from the rear, and without manipulation of the arm.

Under the second method, if the patient offers resistance, he ordinarily starts forward, or, if sitting, he attempts to rise, thus assisting the surgeon.

REVIEWS.

INTERNATIONAL CLINICS. Edited by A. O. J. KELLY, A.M., M.D., with the assistance of collaborators and correspondents. Vol. IV., pp. 321. Thirteenth series. Philadelphia: J. B. Lippincott Co., 1904.

THIS volume presents many subjects of importance and interest to practitioners, even though they are working within narrow lines. The treatment of Ulcer of the Stomach (Tyson), Infectious (rather than croupous) Pneumonia (Musser), Chronic Bronchitis (Claytor), and Syphilis (Julien) leave nothing to be desired so far as these topics are concerned. In Medicine, Duckworth pleads for a broader view for the student in the Physiognomical Diagnosis; Favill and Bishop concern themselves with the Kidneys; Duncan presents a practical paper on Tropical Dysentery; Satterthwaite continues his work on the heart in presenting well-reasoned-out remarks on Palpitation, Abnormal Rhythm, and the Frequent Pulse; Poynton endeavors to show how far there is a Parallelism between Clinical Symptoms and Pathological Lesions in Rheumatic Fever; Burnet gives a short paper on Angioneurotic Œdema (the literature might have been more profitably studied), and Syphilis as causing Aortitis is the subject chosen by Preble. Thus we find more than a third of the book devoted to Medicine and the subjects well and adequately presented from the standpoint of the physician.

In Surgery there is indeed a surfeit of the rare and recent. Keen and Da Costa, Senn, Albarran, Coomes, Battle, and Dugan, offering real advances on many topics, should satisfy the surgeon.

In Gynecology and Obstetrics four papers by Davenport, Wiggin, Pinard, and Frank, on both minor and major matters, possess much interest. James takes up Hemiplegia; Brewer reports an instance of Cerebral Hemorrhage and Right-sided Hemiplegia without Aphasia, and discusses Multiple Sclerosis and Delirium Tremens, offering much that will interest the general practitioner.

Orthopedics is represented by a single article by Porter on Congenital Dislocation of the Hip, Infantile Cerebral Paralysis, and Congenital Clubfoot.

In Ophthalmology, Wood on the Preparation of the Patient for Cataract Extraction, and Nolude on the Diagnosis and Treatment of Acute Glaucoma, furnish substantial information.

Of great present interest is the last paper, by McFarland, on the Present State of our Knowledge of Immunity, in which he endeavors to reconcile, imperfectly, as it seems to us, the theories of Metchnikoff and Ehrlich. Nor do we find the clearness and conciseness which has marked other contributions. Further, the diagram on page 298, borrowed from Grünbaum, needs further explanation than that vouchsafed by the writer for complete comprehension by those not familiar with the original. However, as a statement of our present notions regarding what has been the *crux* of both laboratory and clinical workers in this field, we may regard this as satisfactory. As each volume comes before us we are more and more impressed by the energy of the editor and his assistants in gathering really good work by distinguished men. In marked contrast to the deluge of communications which we are obliged to read and in reading know that their value can be but ephemeral, these contributions to medicine and surgery are distinctly grateful.

R. W. W.

INFECTIOUS DISEASES: THEIR ETIOLOGY, DIAGNOSIS, AND TREATMENT. By G. H. ROGER. Translated by M. S. GABRIEL, M.D. Illustrated with 43 engravings. Philadelphia and New York: Lea Brothers & Co., 1903.

AMIDST the great mass of stereotyped text-books it is truly refreshing to find a treatise upon the infectious diseases designed so as "to harmonize any seeming antagonism between experimental research and clinical observations, and to reduce the theories of infection and immunity to the basis of practical utility." The idea is enticing, and one is led to expect so much that an actual perusal of the book is somewhat disappointing. The classification of infections is itself rather artificial, and it is difficult to see upon what grounds yellow fever should be classed as a specific bacterial infection localized in the liver.

In the portion devoted to "nodular infections," the discussion on tuberculosis is in the main good, but the rest of the chapter, which deals with pseudotuberculosis, oidiomycosis, and actinomycosis, leaves certain points unexplained. Under the bacterioscopical examination of the blood one is surprised to find the statement that in typhoid fever the typhoid bacillus "is only very exceptionally encountered in the blood of the general circulation." Again, the conclusions which the author draws upon the etiology of dysentery are not at all in accord with the results of the latest researches upon this subject made in Japan, Germany, the Philippine Islands, and in this country.

A large portion of the book is devoted to a discussion of the "influence of infections upon the organism." Many of these chapters are excellent, and the general conception and treatment of this portion of the book is noteworthy. The sections upon the hæmopoietic organs, nervous system, and development of arteriosclerosis contain much that is new and valuable. The subject of fever in general is ably dealt with, and the author's original researches upon appendicitis, variola, and bone-marrow lend special interest to these subjects.

Of the 850 pages almost 300 are devoted to the treatment of infectious diseases. Naturally much space is given to serum-therapy. The book is valuable and worthy of careful study.

W. T. L.

CLINICAL TALKS ON MINOR SURGERY. By JAMES G. MUMFORD, M.D., Assistant Visiting Surgeon to the Massachusetts General Hospital, and Instructor in Surgery, Harvard University Medical School. Boston: The Old Corner Bookstore.

THIS little volume of *Clinical Talks on Minor Surgery* is most readable and is full of valuable information. It tersely presents the up-to-date treatment of minor surgical conditions. It is composed of ten lectures, each of which presents a number of important lessons for the student, and even the experienced surgeon can read them with profit. In the recent unparalleled advancement of surgery too little attention has been paid by teachers and writers to the lesser surgical ailments, and yet these conditions are those which fall to the general practitioner for treatment. Every student and every general practitioner will find in these few pages the recent advances in minor surgery delightfully presented. We can heartily endorse what the author has to say about the treatment of sprains, fractures, and dislocations.

J. H. G.

HANDATLAS DER ANATOMIE DES MENSCHEN. Mit Unterstützung von WILHELM HIS, Professor der Anatomie an der Universität, Leipzig. Bearbeitet von Werner Spalteholz, ao. Professor an der Universität Leipzig und Custos der Anatomischen Sammlungen. Dritter, Band 2. Abtheilung. Leipzig: Verlag von S. Hirzel, 1903.

THIS portion of Spalteholz's *Hand Atlas of Human Anatomy* deals with the nervous system and organs of special sense. We had not the pleasure of reviewing the former portions of this work,

but of the present volume we can speak in the highest praise. It consists of beautiful illustrations of the entire nervous system, of the eye, the ear, and the nose. The text is full and descriptive. The illustrations are among the best which we have had the pleasure of seeing, and as an atlas the work can be highly commended. It is, however, to be regretted that so fine a piece of work should be found in a paper binding. J. H. G.

CRUSADE AGAINST CONSUMPTION. By LAWRENCE F. FLICK, M.D. Philadelphia: David McKay, 1903.

THIS little volume is, according to the author, offered to the public for the purpose of bringing about a clearer understanding of consumption. It is divided into forty-six chapters, each dealing with important questions which relate to the disease. As examples may be mentioned: What Consumption is; Diseases which Predispose to Consumption; How Tuberculosis is Spread by Contact with the Consumptive; Public Conveyances in the Spread of Tuberculosis; The Prevention of the Spread of Tuberculosis; Should Consumptives Marry?

The arrangement is simple and the terms popular, so that the subject-matter is quite within the grasp of the average layman and would certainly render him far more capable of aiding the medical profession in combating the disease.

While we may not agree with Dr. Flick in some minor statements, the work as a whole is an excellent one for the purpose, and we hope it may be widely circulated. T. A. C.

DISEASES OF THE NOSE AND THROAT. By CHARLES HUNTOON KNIGHT, A.M., M.D. Philadelphia: P. Blakiston's Son & Co., 1903.

THIS work, based upon Dr. Knight's lectures to students at Cornell University, can be consulted with profit not only by the undergraduate, for whom it is intended, but also by those who are doing more advanced work in the treatment of diseases of the nose and throat. Dr. Knight is well known as one of the most progressive workers in this special field in this country, and these lectures, embodying his own personal experiences and observations, are consequently possessed of great value to the specialist in laryngology. The author has wisely omitted going into the detailed anatomy of

the nose and throat, referring the reader to larger works or to anatomical writings for the minutiæ of the subject. Throughout the entire work the author's effort at conciseness is visible, and its results have been most happy. Everywhere he utilizes his space to the fullest extent to bring out valuable practical points to the exclusion of unnecessary details. The illustrations, probably because many of them are taken from standard works, are above reproach. Taken as a whole the book may be regarded as a thoroughly up-to-date, concise presentation of the most important facts in laryngology and rhinology. F. R. P.

A Text-book of Clinical Anatomy for Students and Practitioners. By Daniel N. Eisendrath, A.B., M.D., Professor of Clinical Anatomy in the Medical Department of the University of Illinois (College of Physicians and Surgeons); Attending Surgeon to the Cook County Hospital, Chicago; Professor of Surgery in the Post-Graduate Medical School, Chicago. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

The teaching of anatomy has during recent years undergone considerable improvement, but none is more notable than the teaching of applied anatomy to advanced students. It is a great mistake to allow a student to think that when he has passed his examinations in descriptive anatomy at the end of his second year that he is then possessed of all the anatomical knowledge necessary for the practice of medicine and surgery.

The object of the author of this book is to present to these advanced students and to practitioners the anatomical knowledge necessary to the successful practice of general medicine, surgery, or any of the specialties. Consequently, the book deals largely with topographical and relational anatomy. Such a work, in order to meet the demand of the reader, must present numerous and good illustrations, and with these the present work is well supplied. The longitudinal and transverse sections of the various regions of the body are well reproduced and serve a good purpose.

A criticism which might be offered on the illustrations is that there are a number of them repeated several times in the book. This is supposedly done for the convenience of the reader, and on this ground may be excused.

The text is lucid and its arrangement well adapted to the study of clinical anatomy. The profession, and particularly the teaching profession, should welcome the issue of books of this kind, and

the present volume meets with our hearty commendation, as it is sure to be a great aid to both the student and the practitioner.

J. H. G.

THE DIAGNOSIS OF DISEASES OF WOMEN. A TREATISE FOR STUDENTS AND PRACTITIONERS. By PALMER FINDLEY, B.S., M.D., Instructor in Obstetrics and Gynecology, Rush Medical College, in affiliation with the University of Chicago; Assistant Attending Gynecologist to the Presbyterian Hospital, Chicago. Illustrated with 210 engravings in the text and 45 plates in colors and monochrome. Philadelphia and New York: Lea Brothers & Co., 1903.

THIS is a well-written and beautifully illustrated book of about 500 pages. It should be in the hands of all who are making a special study of gynecological pathology. Special stress is laid upon microscopic diagnosis of the various lesions in Part II., and here the subject of the diagnosis of malignant processes is particularly well handled. The author has collected the thought of the best authorities, to whom credit is given, and has presented in a comprehensive and practical manner a great deal of information which cannot be obtained from general text-books on gynecology. While the book is handsomely illustrated, it contains many illustrations which are superfluous. Some of those of sounds, curettes, specula, dilators, tenacula, sponge tents, operating tables, etc., are unnecessary, and the views illustrating the different positions, etc., might with propriety be omitted in a book designed for advanced students.

J. B. S.

AN ATLAS OF HUMAN ANATOMY FOR STUDENTS AND PHYSICIANS. By CARL TOLDT, M.D., Professor of Anatomy in the University of Vienna, assisted by ALOIS DALLA ROSA, M.D. Translated from the Third German Edition and adapted to English and American and International Terminology by M. EDEN PAUL, M.D. BRUX., M.R.C.S., L.R.C.P. First Section: A. The Regions of the Human Body; B. Osteology. Second Section: C. Arthrology. New York and London: Rebman Company, 1903.

UNDER the head of Regional Anatomy, Toldt presents an atlas of human anatomy for students and physicians. The work is a translation by M. Eden Paul from the third German edition. The first two parts of this work are before us for review.

The first part deals with Osteology and is preceded by about ten pages of illustrations representing the various regions of the human body. There is no text, the anatomical points of interest being indicated on each bone. The cross-sections of the bones are particularly good. We feel, however, that this section of the work could be greatly improved by having the muscular and ligamentous attachments indicated on the bones, as is done in colors in so many of the recent works on anatomy.

The second part of this work presents the various articulations of the human frame. Its style is exactly that of the first part of the work; but in this some coloring of muscular attachments is presented.

The illustrations are so numerous and so good that it would be impossible for a student reading a description of a bone to fail to understand it with these cuts before him.

The volumes are of convenient size, and certainly must prove of great value to the student in the study of anatomy. J. H. G.

A Text-book of Surgery for Students and Practitioners. By George Emerson Brewer, A.M., M.D., Lecturer on Clinical Surgery at the College of Physicians and Surgeons, Columbia University, New York; Attending Surgeon to the City Hospital; Junior Surgeon to the Roosevelt Hospital, etc. New York and Philadelphia: Lea Brothers & Co., 1903.

Although it is difficult for an author who undertakes to write a limited single-volume text-book on general surgery to avoid criticism at the hands of reviewers, we feel that Brewer has in this work presented as generally satisfactory a treatise as possible. He has called to his assistance several authorities on special subjects, such as surgical pathology, genito-urinary diseases, and orthopedics. The work was not prepared for the instruction or guidance of the surgeon, but for the student and the medical man who is obliged to occasionally treat surgical conditions, and the author is to be congratulated upon the accomplishment of his object.

One thing which especially strikes us in this book is its thorough up-to-date character. It is well written, very comprehensive, and a reliable guide. It is of necessity brief in many respects, but the author's terseness does much to forestall criticism in this respect. The illustrations are well chosen and good.

The chapter on Fractures meets with our hearty approval, though we cannot refrain from criticising the author for not urging early and continuous passive movements of the fingers in fractures of the

lower end of the radius. This criticism, however, is applicable to a large number of text-books on general surgery.

We can commend this work very heartily to all medical students, since it is one of the best books of its size on the general surgery of to-day which we have seen. J. H. G.

BERICHT UEBER DIE LEISTUNGEN AUF DEM GEBIETE DER ANATOMIE DES CENTRALNERVENSYSTEMS IN DEM JAHREN 1901 UND 1902. Von PROF. DR. L. EDINGER und DR. A. WALLENBERG. Leipzig: S. Hirzel, 1903.

THIS valuable book is arranged as an extensive and comprehensive critical review of recent investigations upon the central nervous system, with special regard to anatomy. The bibliography, composed of over 600 references, includes articles published from all parts of the world, but these are so arranged that within a few pages one can readily find most of the work which has been done on any one subject. All references are given with full titles.

The work is divided into a number of sections. These deal with "Text-books," "Methods of Investigation," "Histology of the Nerve Cell," etc. The main anatomical divisions of the brain and spinal cord are considered under separate headings, and under these main sections subdivisions are again made. The book ends with a section upon the nervous system of the lower vertebrates.

The general method of abstracting the articles is that adopted in the critical reviews of Schmidt's *Jahrbuch*. All the reviews are clear, concise, and very satisfactory. W. T. L.

THE PRACTICAL MEDICINE SERIES OF YEAR BOOKS. Comprising Ten Volumes on the Year's Progress in Medicine and Surgery. Issued monthly, under the general editorial charge of GUSTAVUS P. HEAD, M.D., Professor of Laryngology and Rhinology, Chicago Postgraduate Medical School. Vol. IX.: Physiology, Pathology, Bacteriology, Anatomy. Dictionary edited by W. A. EVANS, M.S., M.D.; ADOLPH GEHRMANN, M.D.; and WILLIAM HEALY, A.B., M.D. Chicago: The Year Book Publishers, 1903.

THE second volume of the Year Books devoted to Physiology, Pathology, etc., is arranged in much the same manner as the first volume, but perhaps shows an improvement in certain particulars.

Investigations upon subjects which have attracted most attention during the year are brought together and reviewed in single paragraphs or sections, so that a general idea gathered from many authorities is given of the advance made in one particular line of research. Many of the reviews are quite long and illustrations from the original articles are sometimes reproduced. Although a uniform method of reference is not adopted, still the references are, as a rule, sufficiently complete to be of use. The addition of an author's index and short dictionary of new words is certainly in place. It is to be regretted that foreign literature is so glaringly neglected. American and English journals are quoted extensively, but the work from French, German, Italian, and Russian authorities receives but little recognition. W. T. L.

PRACTICAL HANDBOOK OF THE PATHOLOGY OF THE SKIN. AN INTRODUCTION TO THE HISTOLOGY, PATHOLOGY, AND BACTERIOLOGY OF THE SKIN, WITH SPECIAL REFERENCE TO TECHNIQUE. By J. M. H. MACLEOD, M.A., M.R.C.P., with eight colored and thirty-two black and white plates. Philadelphia: P. Blakiston's Son & Co., 1903.

ALTHOUGH the skin presents greater opportunities than any other organ or tissue of the body for the study of the processes of disease, the pathologist has made but comparatively limited use of these opportunities. The student of dermatology, therefore, finds but scanty and incomplete information in most text-books of pathology concerning the tissue-changes characteristic of cutaneous disease. The appearance of manuals like the one before us is to be hailed with satisfaction, not only because it is an indication of the scientific spirit with which the study of diseases of the skin is being pursued to-day, but still more because such books will teach the student as he has never been taught before the real nature of the pathological processes taking place in the skin.

The first few chapters of this handbook are devoted to the consideration of microscopic technique, more particularly to the special methods of fixation and staining useful in the study of normal and diseased skin. In the subsequent chapters the general pathology of the several anatomical divisions of the skin—the epidermis, the corium, and the appendages of the skin—is carefully described, special diseases being referred to only as they afford examples of the many lesions peculiar to diseases of the skin. A chapter is given to the technique of blood examinations and the blood changes found to accompany certain diseases of the skin, and to the significance of these changes. In the concluding chapters of the book the bac-

teriology of the skin is considered at some length. The various pathogenic fungi found in and upon the skin are described, together with the numerous staining and culture methods best adapted for their demonstration and study.

Numerous well-made illustrations, most of which are original, are scattered throughout the book, which materially add to its value as a text-book.

The plan of preceding the descriptions of the morbid anatomy of a part by a succinct account of its normal histology seems to us a most excellent one; as a matter of course, a knowledge of the normal structure of a tissue *must* precede an understanding of the alterations produced by disease.

In conclusion, we have only words of praise for this handbook, which we believe ought to be in the hands of every student of dermatology. M. B. H.

TRAITE DE RADIOLOGIE MEDICALE. Edited by CHARLES BOUCHARD, Professeur de l'Institut, Professeur de Pathologie générale à la Faculté de médecine. Paris: G. Steinheil, 1904.

THIS treatise is in two large quarto volumes, containing almost 1100 pages of text and illustrations, and deals with the subject in great detail. Chapters have been written by numerous writers from the most prominent faculties of France. The opening chapters consider the sources and variety of electricity and of electric apparatus, a large space being devoted to the consideration of the Crookes tube and the physical and chemical properties of *x*-rays.

Book II. deals with the practical application of *x*-rays in medicine and surgery. The question of radiographic plates, their preparation, exposure, and development, is minutely treated.

The technique of fluoroscopic examinations and of skiagraphic procedures receives a thorough discussion, with numerous well-executed illustrations of apparatus, and next follows a treatise on "Stereometry and Stereoscopy." A large space is devoted to the study of the practical application of the *x*-rays in surgical conditions —fractures, osteitis, myelitis, acromegaly, orthopedics—and tumors of bone, luxations, arthritis, gout, rheumatism, and the arthropathies are thoroughly investigated. Following these are the examinations of the viscera, the vascular and nervous systems, the special senses, and obstetrical and fetal radiography. An interesting and instructive chapter follows on the accidents of radiology, and particularly of *x*-ray dermatitis and of burns. A remarkable feature of this enormous work is that only eleven pages are devoted to "Radiotherapy." No attempt has been made to describe methods of procedure, but a résumé of some diseases treated and the general

results reported are mentioned. Other diseases the writer declines to discuss, on the ground that they are still in too experimental a stage for conclusions.

The book is an interesting exposition of a vast amount of investi gation, but it is not presented in a form that would render it available for the ordinary practitioner. F. F.

THE PRINCIPLES OF "OPEN-AIR" TREATMENT OF PHTHISIS AND OF SANATORIUM CONSTRUCTION. By ARTHUR RANSOME, M.D. London: Smith, Elder & Co., 1903.

THE present agitation for a more rational treatment of tuberculosis has called out a crop of semi-popular literature, of which this little book is a fair sample. While the author aims to set forth the principles upon which the open-air treatment—chiefly in sanatoria—should be based, and addresses himself to physicians, the style of the book is such as to make it appeal rather to the general public than to the medical profession. Except that it contains useful practical directions about hygiene, clothing and the like, and for the construction of a sanatorium, it has no special interest for practitioners. But anything that tends to popularize the knowledge of what has already been achieved by modern methods of treatment and what there still remains to be done, not only by the profession, but by municipalities and the general public also, deserves cordial commendation. R. M. G.

THE EXACT SCIENCE OF HEALTH BASED UPON LIFE'S GREAT LAW. By ROBERT WALTER, M.D. New York: Edward S. Werner Publishing Co. London: Kegan Paul, Trench, Trubner & Co., Ltd.

THE best that can be said of this publication is that the writer's purpose is probably sincere and that its practical teaching, which resolves itself into the principle of non-interference in disease, is not actively harmful. The style reminds one forcibly of that of Mrs. Eddy's book, and the matter is scarcely more intelligible. It bristles with scientific inaccuracies and still more mischievous perversions and misinterpretations of facts. The author is, no doubt, a conscientious carer for the sick, and has some practical notions on treatment, especially the methods collectively known as physiologic therapeutics; but for the comfort of the reading public we trust he will stick to his practice and leave the writing of books to those who are better versed in the craft. R. M. G.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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Studies in Pneumonia and Pneumococcus Infections.—ROSENOW (*Journal of Infectious Diseases*, March 19, 1904, p. 280), in a review of the literature on the frequency of pneumococcus septicæmia in pneumonia, emphasizes the fact that the results of different investigators show the greatest possible variation. These range from the total failure of the Klemperer brothers to isolate the pneumococcus from the blood in any of their cases to Prochaska's successful isolation of the organism in every one of 50 cases of pneumonia. The latter investigator laid no stress on the degree of dilution of the blood. Of his 50 cases, only 12 ended fatally.

Rosenow found a pneumococcæmia in 132 out of a total of 145 cases of pneumonia in which he took blood cultures. The pneumococcus was demonstrated in the blood in 4 cases before a positive diagnosis could be made, and in obscure cases of pneumococcus infection he thinks that blood cultures may be a diagnostic method of positive value. He is rather inclined to the view that in certain instances lobar pneumonia may be a secondary localization of a primary blood invasion. Rosenow agrees with Fraenkel, Prochaska, and others that the presence of pneumococci in the circulating blood is of no special prognostic value in pneumonia, because he holds with them that a pneumococcæmia occurs in practically all cases. There was a mortality of 40 per cent. in his series. He holds that the higher percentage of successful cultivations of the pneumococcus from the blood is due to recent improvements in technique, namely, the use of large quantities (5 c.c. to 7 c.c.) of blood in liquid media, especially bouillon, and of high concentration of blood instead of high dilutions to overcome the so-called bactericidal action of the blood.

The number and viability of the pneumococci in the blood at the time of the crisis is lessened. Rosenow believes that a leukocytosis is a favorable sign, as the number of leukocytes is a measure of the power of

resistance of the individual. A leukopenia following a leukocytosis is an unfavorable indication, pointing as it does to an exhaustion of the resisting powers. The leukocytosis is probably incited by soluble substances liberated by the pneumococci.

Pneumonic blood and serum behaves as fresh normal blood does in having no bactericidal influence on the pneumococcus. The writer found that agglutination of the pneumococcus by pneumonic serum was constant. He demonstrated that the pneumococcus grown in pneumonic serum produces an acid, and offers the suggestion that some of the toxic symptoms of pneumonia may be due to acid intoxication. The viability and virulence of the pneumococcus are preserved for a very long period upon blood-agar, the hæmoglobin being the constituent most likely responsible for this effect. Rosenow finds that blood-agar plates are valuable for the differentiation of pneumococci and streptococci.

Paralysis Agitans.—HART (*Journal of Nervous and Mental Diseases* March, 1904, p. 177) has made a clinical study of 219 cases of paralysis agitans occurring in Dr. M. Allen Starr's clinic since 1888. There were 139 men and 80 women. The earliest case was in a male, aged twenty-two years; the latest in a male, aged seventy-eight years. The largest number of cases, 40 per cent., began in the decade between fifty and sixty years. Occupation seemed to have no etiological bearing. Direct hereditary transmission can rarely be traced. In only 16 per cent. of the cases could paralysis agitans be found to have existed in relatives. Emotional influences were believed to have been the exciting cause in 40 of the cases. Next to emotion, traumatism seemed the most conspicuous predisposing factor, such a history being obtained in 31 cases. Other contributory causes given are certain acute infectious diseases, overwork, and alcoholism. Syphilis apparently played an unimportant part, and was admitted in only 2 cases. The writer states that the true etiology of the disease is not at all well understood.

Tremor was noted in 203 of the cases. The onset was seven times as frequent in the upper as in the lower extremity, and was more frequent on the right side of the body. In 3 cases it began in the head. It is usually lessened by voluntary motion. Muscular rigidity was present in 142 cases. Contractures were noted in 28 cases. In 173 instances the tendency of the patient to fall was tested. It was absent in 68 and present in 105 cases. The deep reflexes were investigated in 188 cases. Of these, 90 were normal; in 30 they were present but diminished; and in 68 they were more active than normal. There were definite voice changes of varying character noted in 120 cases. Pain in some part of the body was present in most of the cases. Paræsthesias were present in 120 cases also. These consisted usually of "prickling," "numbness," "tingling," "flushing," and "heat and cold." Hyperidrosis was present in 57 instances. The complications varied and could not be said to be dependent on the nervous disease. Two of the cases had hemiplegia.

The treatment was unsatisfactory and there were no cures. An effort in all cases was made to remove sources of anxiety and worry; to place the patient on a simple diet and to improve the general nutrition. The cases which showed most improvement were given massage, passive movements, and hydrotherapy. Medicinally, hydrobromate of hyoscine

and sulphate of duboisine gave the best results. For a time at least they diminished the tremor and relieved insomnia.

On Black Urine.—A. E. GARROD (*Practitioner*, March, 1904, p 383) prefaces an interesting paper on the above subject, with an historical account of the condition. Black urine was described by Hippocrates and others before him. The data in these early cases are too meagre to afford a plausible explanation for their causes. In some of the later cases the descriptions are sufficiently full to conclude that hæmoglobin or admixture of blood, bile pigments, coloring matters from eating certain fruits, and the abnormal constituents of the urine in alkaptonuria were the causes of the discoloration.

Garrod states that in the following conditions the urine is dark-colored on voiding or becomes black on standing: (1) in cases of jaundice, especially when of long standing; (2) hæmaturia; (3) hæmoglobinuria; (4) hæmatoporphyrinuria; (5) melanotic sarcoma; (6) alkaptonuria; (7) ochronosis; (8) in cases in which abundance of indican (indoxyl sulphate) is present; (9) in certain cases of phthisis, only after standing for some time; (10) in certain rare cases of undetermined nature; (11) after the taking of certain drugs and articles of diet (including carboluria). In only a few conditions, such as alkaptonuria and melanuria, does the urine become actually black, and then only on standing.

Some of the above conditions are deserving of special comment. In hæmatoporphyrinuria the urine is usually of a port-wine color, but may be actually black. The color is only in part due to the hæmatoporphyrin. There are other dark abnormal pigments present. The great majority of the cases of this condition are due to the toxic action of overdoses of sulphonal and its allies. Hæmatoporphyrin is recognized by certain characteristic absorption bands on spectroscopic examination.

The melanuria of melanotic sarcoma is rare, and Garrod supports the observation of others, that it does not occur when the growth is limited to its primary seat or to a neighboring group of lymphatic glands, but only when the internal viscera, particularly the liver, are involved. The urine is usually of a normal color when passed, but darkens from the surface downward on exposure to the air. The addition of nitric acid to the cold urine at once produces blackness. Ferric chloride also causes immediate blackening and a gray precipitate which forms is redissolved by an excess of the reagent.

The urine in alkaptonuria behaves in the same way as that in melanuria does on exposure to the air. The darkening is hastened by the addition of an alkali. The urine reduces Fehling's solution and ammoniacal silver nitrate solution in the cold. It does not reduce bismuth solutions and does not ferment, and is thus distinguishable from diabetic urine. The abnormal substance which produces the characteristic reaction is homogentisic acid, first discovered by Baumann and Wolkow.

In the rare condition known as ochronosis, or pigmentation of the cartilages, first described by Virchow in 1866, the urine may be dark in color. Of 7 cases reported, the urine darkened in 3. In 2 additional cases recently reported by Osler the patients were also shown to be alkaptonurics. Garrod thinks, however, that homogentisic acid is not the only substance causing blackening of the urine in ochronosis.

The writer states that although the dark urine of indicanuria is not of infrequent occurrence, it is not so well recognized as it should be. He believes that many cases are mistaken for other conditions, and particularly for melanuria. The color is not due to the indigo pigments nor to indoxyl sulphates, which are colorless substances, but, as Baumann and Brieger showed, to higher oxidation products of indol. These urines blacken when warmed with nitric acid, but there is no such immediate blackening in the cold, as with true melanuria. They do not blacken with ferric chloride, and by this test they may be at once distinguished from those containing melanogen. Any morbid process which leads to abundant excretion of indican may give rise to such urine, as, for example, intestinal obstruction from any cause, excessive bacterial activity in the intestine, or putrefactive changes in collections of pus.

SURGERY.

UNDER THE CHARGE OF

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The Significance of the Zoological Distribution, the Nature of the Mitoses, and the Transmissibility of Cancer.—BASHFORD and MURRAY (*The Lancet*, February 13, 1904) state that within the past year specimens of malignant new-growths have accumulated from all the domesticated animals and from many other vertebrates. The clinical, pathological, anatomical, and microscopic characters of these new-growths are identical with those found in man in all essential features, although the animals themselves are drawn from the different classes of the vertebrate phylum. Stated generally, it may be said that malignant new-growths are frequent according as animals are carefully examined, and are unrecorded in forms which are difficult to examine or do not reach old age in considerable numbers. The figures are not sufficiently extensive to determine accurately the age incidence of the various types of new-growths in different animals, but a relatively higher incidence in old age is apparent.

In regard to the phenomena of cell division in malignant new-growths the following points are of great importance: A complicated sequence of cell changes has been found to be characteristic of carcinoma and sarcoma alike. This sequence is the same as that which initiates the origin of the sexual generation in plants from the asexual, and is terminal in the history of the sexual cells in animals. It must be noted also that all the cells of the malignant new-growths do not undergo the reducing division; a certain number differentiate in the direction of the tissue

among which they have arisen, and in the secondary growths, when present, somatic mitoses occur in the growing margin, which, it will subsequently be shown, is also a feature in the growth of cancer when transferred to a new host.

The transmission of cancer from man to animals, or from one animal to another of a different species, has never been successfully performed. Successful transplantation experiments have been made, however, from animals suffering from malignant new-growths to others of the same species. Careful microscopic examination has clearly demonstrated that the new tumors which develop arise from the actual cells introduced. Transplantation is, in fact, identical with the process of metastasis, as it occurs in the individual providing the tumor. It is remarkable, however, that the tumor used in these experiments does not produce metastases naturally, and its malignancy is only evidenced by its progressive growth and the undifferentiated character of the cells. The process is in no sense an infection, the tissues of the new host not participating in the formation of the new parenchyma. The origin of the stroma has not been accurately determined. The experimental transmission of carcinoma shows that we must distinguish between the problem of the genesis of a malignant new-growth and that of the conditions which permit of its continued existence.

The wide zoological distribution of malignant new-growths—its limits are not yet determined—indicates that the cause of cancer is to be sought in a disturbance of those phenomena of reproduction and cell life which are common to the forms in which it occurs. Our observations on animals show that malignant new-growths are always local in origin and of themselves produce no evident constitutional disturbances whatsoever. These facts are in full accord with accumulated clinical experience in man. In connection with diagnosis and statistics one must emphasize the importance of the absence of specific symptoms. The evidence we have advanced that cancer is an irregular and localized manifestation of a process otherwise natural to the life cycle of all organisms probably explains why it is that malignant new-growths, and their extensive secondary deposits *qua* cancer, are devoid of a specific symptomatology.

Remarks on Extensive Carcinoma of the Œsophagus, with Unusual Nervous Complications.—SAUNDBY and HEWETSON (*British Medical Journal*, March 12, 1904), after reporting in detail this case, state that it is of special interest because it appears to constitute an exception to "Simon's Law": The occurrence of an isolated paralysis of the abductor filaments of the recurrent laryngeal nerve in cases in which the roots or trunks of the spinal accessory, pneumogastric, and recurrent nerves are injured or diseased is not an isolated pathological curiosity. There is a distinct proclivity of the abductor fibres to become affected in such cases, either at an earlier period than the adductor fibres or even exclusively." In this case, both physiologically and pathologically, the adductor disablement was earlier and more intense in degree than the abductor. The clinical evidence showed that this adductor paralysis was an early and constant feature of the laryngeal condition during the whole of the patient's life in hospital. The abductor muscles, on the other hand, appeared to act well until a few days before death, when a slight narrowing of the previously wide-open glottis was noticed.

The most reasonable explanation of this is that the nerve fibres going to the adductors of the vocal cords were disabled earlier and in much larger proportion than the nerve fibres going to the abductor muscles. This explanation, of course, takes for granted that the nerve fibres of the trunk of the recurrent laryngeal nerve are differentiated into special fibres for special muscles, though not necessarily arranged in any special position within the epineurium of the nerve.

Reflex Disturbances Associated with Adherent Prepuce.—SIMON (*British Medical Journal*, March 12, 1904) notes briefly three interesting cases in which marked symptoms were produced by an adherent prepuce, or narrowed urethral meatus. The first case was a boy, aged eighteen months, who suddenly became unable to walk. Any attempt to make him walk caused very severe pain. Careful examination failed to show any coxalgia, but the prepuce was found to be long and adherent. The child was circumcised, and recovery was immediate and complete. The second case, a boy aged fourteen years, had obstinate and severe intestinal colic, which was not relieved by medical treatment. An adherent prepuce being discovered, this was treated, and all the symptoms disappeared. In the last case, a boy aged three years, there was a history of his wakening at night, screaming and complaining of pain in the abdomen. No other cause being discovered, the penis was examined, and the prepuce found adherent and the meatus narrow. Under appropriate surgical treatment the symptoms disappeared.

Experimental Nephritis Followed by Decapsulation of the Kidney.—HALL and HERXHEIMER (*British Medical Journal*, April 9, 1904) state that when Edebohls first suggested the decapsulation of the kidney as a reasonable method of treatment in chronic nephritis he based his proposal upon the urinary and general improvements which followed the fixation of a movable kidney by the removal of its capsule. In one of his cases which died four months after decapsulation, he observed "enormously dilated and enlarged bloodvessels which penetrated from the fatty capsule through the capsule proper into the kidney substance." This access of additional blood he considered would provide increased nutrition, stimulate an extensive regeneration of the secreting cells, and consequently produce a more efficient excretion of waste products. Whether decapsulation yields better results than the simpler reni-puncture of Reginald Harrison, which has been so widely and successfully employed, is a question which the available clinical data have not yet satisfactorily answered. We must wait from two to five years before making any definite conclusions as to the value of this operation. Meanwhile, we may with advantage investigate the anatomical aspect of the procedure, and thus the present inquiry has for its main object the observation of the tissue changes which follow the decapsulation of kidneys in which nephritis has been induced.

While we must clearly admit that artificial animal nephritis cannot be too closely compared with nephritis in a human subject, yet we submit that the changes produced by metallic poisons are somewhat similar in each case, and the experiments provide at least some grounds for the probable occurrence of like processes in the human kidney.

We must, of course, for the moment only deal with the forms of degen-

erative nephritis, as it is yet impossible to induce an interstitial nephritis in animals. From the anatomical standpoint yielded by our experiments and those previously reported, decapsulation does not appear to offer any advantages. And if there exists no anatomical basis for the operation in acute degenerative nephritis, it is surely impossible that in chronic nephritis the capsular changes will be less marked. If indeed the changes are at all analogous, we should imagine that the laceration, the hemorrhage, and the new formation of the capsule would rather tend to accelerate the interstitial inflammation; while in the event of any concomitant arteriosclerosis there would be no possibility of much vascular anastomosis or even of a satisfactory replacement of the channels ruptured during the removal of the capsule.

But if there is no anatomical basis for the operation, there may be another explanation of the rapid flow of urine—the increased excretion of urea, the disappearance of the albumin and casts which have been observed to follow decapsulation. By some the results are ascribed to the relief of congestion, but in our experiments the intense hyperæmia persisted after the capsule had reformed. Pel, Jaboulay, and others suggest that the improvement is due to the action upon the sympathetic ganglia, and that the decapsulation should be considered in the same light as those operations which, undertaken to remove a renal calculus, lessen the pain and improve the general condition of the patient, although no calculus is found.

If the latter be the correct explanation, the question naturally then arises as to the necessity for the entire denudation of the renal cortex. Would not reni-puncture, or one longitudinal and several transverse incisions, while avoiding the main anatomical disadvantages, afford a sufficient stimulus to the sympathetic centres? We cannot at present offer any experimental evidence upon this point. That it would provide a sounder anatomical basis is probable; at all events, it would more locally limit the interstitial and capsular processes in kidneys, the seat of chronic nephritis.

Guiteras has recently compiled the results of some 120 cases in which the diagnoses of chronic nephritis were fairly well established before decapsulation and their postoperative courses followed for some months. Regarding the results from their most favorable standpoint, 16 per cent. of the total number may be said to be "cured," 40 per cent. thought to be improved, 11 per cent. unimproved, and 33 per cent. followed by early death. Suker reports 15 cases of nephritis in which retinal changes had occurred and which were submitted to decapsulation; 14 died within the "two-year" period, and the history of the remaining one was somewhat questionable.

The value of these statistics is, however, minimized by several considerations. First, the operation has been necessarily restricted to the latest stages of the disease, and has often been only performed as a last hope; secondly, the exact stages and extent of chronic nephritis do not permit of accurate diagnosis; thirdly, chronic nephritis is, as a rule, characterized by acute exacerbations and frequent remissions, its anatomical course is in the main a progressive one, and the remittent stages often occur under treatment other than that of decapsulation.

Of the above 33 per cent. mortality, 26 per cent. died from chronic interstitial nephritis; and of the remainder, in 25 per cent. death occurred

from the so-called chronic parenchymatous nephritis, and in 75 per cent. "diffuse"(?) nephritis was assigned as the cause.

In acute nephritis, anuria, hæmaturia, puncture, and decapsulation of the kidney is said to yield relief and to favorably affect the function of the other kidney. In these cases it is suggested that the improvement is due simply to the relief of tension.

From the standpoint of pathology we may not make an excursion into the field of surgery, and therefore we must not discuss the possibilities of the operation. We feel, however, that the purpose of the paper would not be served unless we mentioned that, while many American and some French surgeons regard the procedure as one that has come to stay and as possessing much promise in the treatment of degenerative and interstitial nephritis, such operators as Israel, Nicolayson, and others have already abandoned the method in chronic conditions. It is, of course, a matter of common knowledge that the simpler renipuncture relieves tension and promotes renal functions; so perhaps the description of the changes observed after decapsulation may give more prominence to the method of simple incision, may emphasize the probability of rapid local reparation when the temporary obstruction is removed, and may suggest the earlier surgical treatment of those postfebrile and acute renal manifestations which, when unrelieved, often terminate fatally.

THERAPEUTICS.

UNDER THE CHARGE OF

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Treatment of Infantile Diarrhœa by Gelatin.—Dr. Weil treats this condition with a 10 per cent. solution of gelatin prepared by adding 10 parts of yellow or white gelatin to 100 parts of boiling water. This is filtered, and while still warm put in test-tubes, into each of which is poured 10 c.c. of the solution. The contents of a tube can easily be added to the patient's feeding, and thus he may get 6 to 8 grams of gelatin per day. The contents of two tubes may be given with each feeding if necessary. In practice it is well to begin with three tubes on the first day and add one each day following. The effects of this treatment are excellent; the stools diminish in frequency, their consistence becomes better, and they gradually come back to the normal type. The color changes from green to yellow, the bad odor disappears, and their reaction becomes alkaline. As the stools become more normal the temperature declines and the general condition is improved. This treatment is not always applicable to acute and chronic types of the disease. It produces regularly good results in the simple gastroenteritis, but when, in addition to the digestive, there are lung, spleen, and liver involvement with albuminuria, the gelatin, while it modifies the stools, does not influence the other conditions.—*Journal de médecine de Paris*, 1904, No. 3, p. 22.

Gymnastics or Massage in Therapeutics.—Dr. Saquet holds that massage is preferable to active movements, especially in joint troubles. In muscular atrophy of so-called articular origin, but which is more likely the result of disuse, massage produces results after several weeks; gymnastics are less important and less rapidly curative when employed alone. It is necessary to remember that in massage normal movements are utilized and these are responsible for the cure. In the paralyses of children massage is found to be more rapid in producing good results than re-education. The results in the aged are less successful. Massage also is to be preferred to re-education in ataxic patients. In general, therefore, massage should be employed in preference to gymnastics, though the latter are successful in a limited number of cases. It is essential, however, that the masseur be a physician.—*Gazette médicale de Nantes*, 1904, No. 2, p. 21.

Ichthargan.—Dr. A. Kronfeld has found that this drug, which is a combination of ichthyol and silver (containing 30 per cent. of the latter and 15 per cent. of sulphur), is a valuable addition to the antiblennorrhagics now in use. Ichthargan is a brown powder, easily soluble in water, glycerin, and dilute alcohol. In acute gonorrhœa, in addition to prescribing rest and proper diet, the author prescribes the introduction once or twice a day of a drainage-tube impregnated with a 0.02 per cent. solution of ichthargan in gelatin. This tube is allowed to remain in the urethra until the gelatin has become dissolved. This usually takes from five to ten minutes. Then the tube is withdrawn. Such treatment is painless and produces good results. In chronic gonorrhœa a 0.02 per cent. solution of ichthargan is used as an injection. The qualities possessed by this drug, which should commend it to use, are its ability to act deep in the tissues, due to its ichthyol content and its astringent and antiseptic properties which it owes to the silver.—*Therapeutische Monatshefte*, 1904, No. 1, p. 32.

Adrenalin in Gynecology.—M. H. Cramer considers that adrenalin 1:3000 applied upon tampons is efficacious in *pruritus vulvæ*. In endometritis solutions of a strength of 1:1000 or 1:2000 applied before cauterization causes an anæmia of the tissues and increase the efficacy of the treatment. The hæmostatic action of the substance makes its application before curettement or the use of the actual cautery useful in inoperable cancer of the cervix. When applied to the ulcerated surface for five minutes upon a tampon saturated with a 1:1000 solution or by an injection into the diseased tissues of about forty-five minims, renders the operation comparatively bloodless. Swabbing the uterine cavity with a 1:2000 solution immediately after curettage produces a complete hæmostasis, which renders inspection through the dilated cervix an easy matter.—*Revue française de médecine et de chirurgie*, 1903, No. 8, p. 184.

Treatment of Ozæna by Injections of Paraffin.—Dr. E. J. Moure employs the following technique in the treatment of this affection. The material used melts at 60° C., although others advocate paraffin of a lower melting point. The syringe has a capacity of forty-five minims, and if its cylinder is of ivory it will be found to conduct the heat less than if of metal. The syringe properly sterilized and heated is filled

with the paraffin, which is injected at a temperature of 55° C. Holding the nasal speculum in place with the left hand, the mucous membrane is punctured and the paraffin slowly injected. Only one puncture should be made, lest the paraffin exude from the one first made. Rarely is it necessary to inject more than fifteen or thirty minims. The posterior portion of the inferior turbinate is the place of election for the puncture, although in certain cases other situations may be employed. Usually a single sitting only is necessary to bring the nasal fossa to its normal calibre, but supplementary injections may be made, if indicated, a few weeks later. In all cases the injection should be made from behind forward. After the operation the odor of the nasal secretion soon becomes less foul and the crusts disappear, although in some cases nasal irrigations may be necessary as an adjunct to the treatment, and in cases of not too long standing complete cure results. The paraffin treatment seems to be superior to any other at present employed. —*La semaine médicale*, 1904, No. 8, p. 61.

Aristochine in Whooping-cough.—Dr. Hermann Kittel sums up his observations in regard to the employment of this drug in whooping-cough thus: He has treated thirty-four patients, of which he considers twenty-five entirely cured. Seven others were improved and in two instances the treatment had not been of sufficient length for inference to be drawn. The duration of the treatment varied from six days to four weeks, and in infants less than a year old the results were particularly startling, the cure taking place very quickly. In older children recovery was less rapid, due, perhaps, to the employment of too small dosage. To achieve the best results treatment should be begun early in the disease. The children under one year old received three times a day one and one-half grains for each month of their age, with fifteen grains as a maximum. Older children were given thirty grains three times a day. In no case was any untoward effect noticed.—*Journal de médecine de Paris*, 1903, No. 52, p. 520.

Collargol.—Dr. Auguste Guerin summarizes various reports upon this drug, as follows: When given by inunction in scarlet fever and measles the patients recover without complications. In fevers it causes an amelioration of the general state and seems to exercise certain resorptive powers. It causes the joint effusion of rheumatism and the effusion of pleurisy to disappear in an extraordinarily short time. In infectious endocarditis it has brought about recovery and seems to modify for the better the course of pneumonia. In typhoid fever and tuberculosis, unfortunately, it has not seemed to give benefit, but in erysipelas, puerperal fever, osteomyelitis, phlebitis, and other pus infections it seems to have a field of usefulness. It may be employed as an intravenous injection in 1 per cent. solution, as a 15 per cent. ointment for inunction, or it may be given internally. The author inclines to the opinion that observers have been, perhaps, oversanguine concerning the drug and concludes that further and scientific observations upon it are needed.—*Journal de médecine de Bordeaux*, 1903, No. 52, p. 845.

Marmorek's Serum in Tuberculosis.—M. Dieulafoy reports upon seven cases treated by this serum. Four of these were patients affected with pulmonary tuberculosis in different stages; two others had in

addition laryngeal involvement, and the seventh was suffering from tuberculous pleurisy with effusion. From seventy-five to one hundred and fifty minims of the serum were injected at each dose, and the injections were given every day, every two days, or at longer intervals. The results were as follows: (1) the serum did not appear to affect the rise of temperature favorably; (2) the sputum often was doubled or tripled in quantity after an injection; (3) in several of the patients neighboring lesions in lungs or pleura seemed to be caused by the treatment; (4) the patients emaciated rapidly in spite of overfeeding. For these reasons the treatment was discontinued. Two of the patients were living at the time of the report, but the others have died. The injections of the serum into inoculated animals seems to produce as unfavorable results as upon human beings.—*Bulletin de l'Académie de Médecine*, 1903, No. 39, p. 365.

Treatment of Croupous Pneumonia with Creosote Carbonate.—Drs. J. A. Scott and Charles M. Montgomery claim that while our methods of treatment of this disease are more humane and founded on a better therapeutic basis, the mortality has not been reduced if we take large numbers of cases into consideration. This report is based upon sixty-seven patients, of whom ten died, a mortality of 14.9 per cent. The amount of the remedy employed was ten to fifteen minims in capsules for adults every four hours. Their conclusions are that (1) creosote carbonate causes no irritability of the stomach; in no case was there vomiting or any disturbance of the digestion; no disturbance of the urine was noted. (2) The degree of toxæmia in all cases, barring the fatal ones, was mild; this is a difficult point to estimate, the extent of lung involved, temperature, etc., having little or nothing to do with it. (3) In the cases treated pseudocrises were common (fifteen), but bore no relation to the crises or to the mortality. (4) The mortality percentage does not corroborate the unusually low figures reported by various observers, nor does it prove that the results were due to the treatment, as equally good results have been secured in past years by other methods in the same hospital. (5) The study of the clinical effects of this remedy should be continued; the dosage should be increased, and the effects on the toxæmia should be carefully watched. —*Therapeutic Gazette*, 1903, No. 12, p. 793.

[The fifth paragraph of these conclusions contains at once a suggestion as to the cause of failure and the method whereby the reporters may lessen their mortality percentage. Attention is directed to the fact that the dose is to be that required, and inasmuch as apparently no harm results from doses many times larger than those cited and the degree of toxæmia is difficult to estimate, larger rather than smaller doses are advised.—R. W. W.]

Adrenalin in Typhoid Hemorrhage.—Dr. Graeser reports the history of a female patient, aged thirty-six years, who had a typical attack of typhoid fever, associated with a bronchopneumonia, or diffuse bronchitis. This patient recovered from the pneumonia, but developed a typhoid-like rash and a typical typhoid temperature. Two weeks after the onset of the typhoid and one week after the appearance of the roseola, an intestinal hemorrhage took place, which was treated with ice, opium, bismuth, and ergot. Bleeding was so extensive as to

threaten death, and adrenalin was used, 30 minims, in saline solution, every three hours, with the result of a sudden cessation of the bleeding, either as coincidental or as causative.—*Münchener medicinische Wochenschrift*, 1903, vol. l. p. 1294.

Effect of Bismuth Preparations in Therapy —Dr. B. Laquer writes that bismuth preparations act, not only mechanically on catarrhal and ulcerative conditions of the mucous membrane of the stomach and intestines, but also chemically, as antiseptics. Bismuth and its preparations, particularly bismuth protoxide, has a marked catalytic power and is capable of diminishing the proteid putrefactive processes in the intestinal tract. Bismuth subnitrate is reduced in the intestine by the action of the intestinal juices to bismuth protoxide, which, in part, explains its beneficial action.—*Archives de médecine des enfants*, 1903, No. 6, p. 340.

Diet in Constipation.—Dr. Henry F. Hughes, as a result of his experience in the Out-patient Department of the Massachusetts General Hospital, discusses this question and presents the following table of diet: Breakfast: Cereal, with cream and sugar—preferably corn meal, or rye and oats; two soft-boiled or scrambled eggs; bread—preferably black bread or pumpernickel, or rye bread, with much butter; fruit, apples or grapes. Dinner: Soup—preferably vegetable soup; fish or meat, or both, with salad; vegetables, at least two kinds—preferably spinach, cabbage, beets, turnips, potatoes, beans or peas, if desired; dessert of rice or bread pudding or custard, including daily a saucer of prunes. Supper: Bread and butter; cocoa; cold meat and vegetable salad; dessert of stewed fruit, apples or pears or figs. If necessary, include a saucer of prunes. Drink at least three pints of water daily.—*Boston Medical and Surgical Journal*, 1903, vol. cxlix. p. 317.

OBSTETRICS.

UNDER THE CHARGE OF

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Septic Infection during Labor and the Puerperal State.—'Jardine (*Journal of Obstetrics and Gynecology of the British Empire*, March, 1904) draws attention to the fact that between the years 1875 and 1895 the number of deaths from puerperal septic infection in Scotland was greater than the mortality had been in what are called pre-antiseptic times. He accounts for this from the fact that at that time anæsthetics were misused and that the free employment of anæsthesia led to the performance of many unnecessary and injurious operations. Anti-

septics were also misused, and indiscriminate douching did great harm. At the present time with aseptic precautions, with as little interference with the uterus as possible, and with the restriction of operations to cases in which they are clearly demanded, the mortality rate is again diminishing.

The Anatomy of Twin Monsters.—BERRY (*Journal of Obstetrics and Gynecology of the British Empire,* March, 1904) describes two cases of twin monsters, with their dissection, in which a study was made of the specimens to determine their mode of development. It was interesting to find that the livers were fused into one and that the hearts were also partially merged into one. In tracing the development of this monstrosity the writer believes that evidences are found to show that bilateral segmentation of a single ovum is necessary for the production of twins, and that so far as the liver is concerned it is developed from a middle portion of the intestine.

Vaginal Cæsarean Section: Three Cases.—MUNRO KERR (*Journal of Obstetrics and Gynecology of the British Empire,* March, 1904) publishes notes of three cases of vaginal Cæsarean section.

The first was in a primipara who had been twenty-four hours in labor. In spite of opium and hot douching, the cervix refused to dilate. In these cases Duhrssen's deep incision was selected, delivery was readily accomplished, and the cervix was closed by catgut stitches. The patient made a very good recovery, with good union. In a case of eclampsia the same method of deep incision of the cervix was successful, the patient recovering with good union. In this instance vaginal Cæsarean section was declined in favor of deep incision.

In the case of a multipara, five months pregnant, suffering from pernicious nausea, the patient suddenly became very ill with continuous vomiting and a very feeble pulse. The cervix was rigid and firmly contracted. Vaginal Cæsarean section was performed by separating the bladder from the uterus. The cervix was then split beyond the internal os and the fœtus and placenta readily removed. The uterus was then irrigated, the womb closed by sutures, the bladder brought down again and held in place by a few stitches. The vagina was packed with gauze. The patient made an uninterrupted recovery.

Kerr also reports a case of eclampsia in a woman in a very critical condition on whom he performed vaginal Cæsarean section. The child was dead when delivered by forceps. There was little bleeding after delivery; the uterus contracted firmly. Injury occurred to the bladder in this case, and the patient recovered with a vesicovaginal fistula.

Retention of the Fetal Skeleton in Utero. — POLANO (*Zentralblatt für Gynäkologie,* 1904, No. 14) reports the case of a multipara, aged thirty-six years, who had had seven normal labors, the last three years before. Menstruation had been interrupted for four months, and there had been repeated hemorrhage. Five days before admission to the hospital amniotic liquid was discharged. In spite of rest in bed and the use of opium, hemorrhage continued without much pain. On the eighth day after admission there was a foul discharge, and the femur of a fœtus was found in the vulva. The uterus was then dilated and the remaining bones of the skeleton were removed.

The Correction of Face Presentation by External Manipulation.—Ostrcil (*Zentralblatt für Gynäkologie*, 1904, No. 14) reports a number of cases in which he has used either the method of Schatz or that of Thorn to correct face presentation early in labor. He was successful in most of these cases. In one of contracted pelvis, the amniotic liquid having escaped twenty hours previously, the chin was behind in the anteroposterior diameter of the pelvis. The effort to correct face presentation was unsuccessful, and the patient was delivered by embryotomy.

Shock or Hemorrhage.—Lomer, at a recent meeting of the Obstetrical Society of Hamburg (*Zentralblatt für Gynäkologie*, 1904, No. 14), described a case of extirpation of the uterus through the vagina at six months' pregnancy for carcinoma. Two-and-a-half hours after operation the patient collapsed, and abdominal section showed a small bleeding vessel, which was secured. The patient recovered.

In another case myomotomy was performed by a rapid and easy operation, the patient suffering from collapse one hour afterward. No sign of hemorrhage could be found, and the patient recovered under a moderate dose of morphia. A case of ruptured ectopic gestation was operated upon without especial difficulty, and the operation was followed by a very brief shock, from which the patient soon rallied.

He also reports the case of a patient, aged thirty-four years, who was taken in labor during the night and who gave birth to a large child fifty-five minutes after she awoke from sleep. There was hemorrhage, which was controlled by gauze packing and ergot. The uterus contracted firmly and the pulse was good, but the patient manifested every sign of fatal shock. Two hours after the packing was removed and replaced and hemorrhage was found to be absent. She slowly recovered.

In discussion, attention was drawn to the fact that in some of these cases no definite reason can be found for the production of the shock which is present.

Depressed Fracture of the Skull Caused by Labor and Its Treatment.—An interesting case of successful treatment for this dangerous complication is reported in the *British Medical Journal*, April 16, 1904, by Ross. The patient was a multipara. Labor had been in progress for fourteen hours without much improvement. The os was fully dilated, the head presented normally and was engaged. Delivery was effected by axis-traction forceps, there being considerable resistance at first, which suddenly yielded. The pelvis was slightly contracted.

There was a deep, almost circular depression, measuring about two inches in each direction across the left frontal bone. The edge of the bone at the anterior fontanelle was slightly tilted up. An effort to raise the depression by placing the head between the knees and making pressure failed. Two days after birth operation was done at the Glasgow Maternity Hospital. An incision one inch long was made through the scalp near the anterior fontanelle, and the bone was cut through. An elevator was then inserted and passed forward between the bone and the dura mater. To avoid injury to the dura mater the incision in the bone was made one-quarter of an inch away from the suture to which it adheres. The inner portion of the bone was raised without difficulty

and a sound and sensation were produced as if a dent in a celluloid ball were being pushed out. A fracture was found and the other fragment was also raised. There was little bleeding and the wound was closed readily with two stitches. The scalp wound healed in four days, the head becoming normal. The child had shown no symptoms following the injury.

GYNECOLOGY.

UNDER THE CHARGE OF

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Position of the Arms during Narcosis. — ROTHE (*Zentralblatt für Gynäkologie*, 1904, No. 12) comments on the comparative frequency of paralyses of the brachial plexus after operations in Trendelenburg's posture, which, he believes, are due to pressure exerted on the plexus at a point between the clavicle and the first rib. Some of these cases resist treatment for months. In addition to these he has noted a number of cases in which minor disturbances followed, such as temporary numbness, crawling sensations, etc.

He has found that all these unpleasant phenomena can be avoided by arranging the arms in a proper manner and at the same time noting the amount of compression to which the arteries are subjected. The pulse at the wrist is a valuable guide. He tried the plan of elevating only one arm, turning the head to the side, but found the same tendency to paralysis of the median nerve as before. Then he tried fastening the arms at the sides, below the table, with a cushion under each arm. This procedure has given the best results.

Prophylaxis of Postoperative Cystitis.—BAISCH (*Zentralblatt für Gynäkologie*, 1904, No. 12) finds that two factors are present in the etiology of this condition: Disturbance of the innervation of the bladder leading to paralysis of the viscus, and interference with the nutrition of the organ, caused by extensive dissection. In addition, staphylococci and bacteria coli present in the urethra are apt to be introduced on the catheter.

In consequence the writer employed irrigation of the bladder after every catheterization, with the best results. Only 1 patient was able to urinate spontaneously after 31 abdominal hysterectomies. Of the 25 patients who survived, 22 were catheterized for twenty-two days without developing cystitis.

The most careful asepsis is necessary in using the catheter, and irrigations (with boric acid or protargol solution) should be continued until the patient is perfectly able to pass her water. In the case of minor operations the ischæmia is transient and less marked.

[In our experience the patient is less apt to suffer from permanent vesical inflammation than from urethritis and irritation at the neck of the bladder, due to the rough or unskilful use of glass catheters.—H. C. C.]

Removal of Ureteral Calculus per Vaginam.—GRADENWITZ (*Zentralblatt für Gynäkologie*, 1904, No. 12) reports the following case: The patient, aged forty-three years, had suffered for three years with colicky pains, beginning in the right kidney and radiating over to the left. She had passed two phosphatic calculi. On vaginal examination a small stone was felt in the bladder, which was easily removed per urethram after moderate dilatation. Four weeks later the patient re-entered the hospital on account of a return of the colicky pains. It was now possible to palpate a stone, the size of a cherry-pit, impacted near the left ureteral orifice. Cystoscopic examination was negative, and the daily excretion of urine was about two pints. Three months later only half this quantity was excreted, and catheterization of the left ureter showed that no urine escaped from that kidney, though the fact of hydronephrosis could not be established.

Under narcosis the usual transverse incision anterior to the cervix was made, the bladder was dissected upward, and the lower portions of the broad ligaments were divided between ligatures, although the uterine arteries were not tied. The stone was fixed by pressure through the abdominal wall, and after further blunt dissection the ureter was drawn down into view, incised, the calculus (uric acid) was removed, and the incision was closed with fine sutures. The patient's convalescence was afebrile, the daily amount of urine at once became normal, and four months later there was no evidence of further trouble.

Histology of Parametritis.—BUSSE (*Monatsschrift für Geb. u. Gyn.*, Band xviii., Heft 1) calls attention to the fact that so-called pelvic exudates differ widely anatomically. In some cases there is a simple œdema of the parametric tissues, in others fibrinous inflammation without marked increase in the leukocytes, such as is noted in the more acute forms. Suppuration follows, with later hypertrophy of the connective tissue and accompanying degenerative changes, especially fatty.

The Action of Oophorin.—MATHES (*Monatsschrift für Geb. u. Gyn.*, Band xviii., Heft 2) asserts that ovarian extract causes an excretion of the phosphates, which is less marked in women whose ovaries have been removed. In general, castration appears to diminish the salts in the body.

Leukocytosis in Diseases of the Pelvic Organs.—DUTZMANN (*Monatsschrift für Geb. u. Gyn.*, Band xviii., Heft 1), continuing his studies of this subject, presents the results in 2000 blood-counts, made in 223 patients. His conclusions are as follows: Leukocytosis is a valuable guide to the presence of pus in the case of pelvic exudates, and furnishes an indication for incision. The iodine reaction of the white cells serves to confirm the diagnosis in a doubtful case of supposed abscess.

In diseases of the adnexa the leukocyte-count not only assists the diagnosis, but guides the surgeon in his choice of the abdominal or vaginal route. In cases of fibromyoma, carcinoma and ectopic gesta-

tion leukocytosis is often the only indication of complicating purulent disease of the adnexa, or possible suppuration of an hæmatocele. Tubercular pus does not cause an increase in the number of leukocytes, and gonorrhœal only moderate, a fact explained by the greater resistance of the peritoneum to the specific organisms of those diseases. A high leukocytosis attends torsion of the pedicle of ovarian cysts, though pus may be absent; the iodine reaction is absent, however.

In septic infection the leukocyte count is especially valuable as regards prognosis, a persistent high leukocytosis being favorable, while a decline is to be regarded in the contrary light. In puerperal sepsis the proper time for interference may be judged accordingly. In eclampsia with hyperleukocytosis the attacks are less frequent, while a decline is noted in a less favorable case. The writer infers from this that in eclampsia there is a true infection (?)

Ovarian Hemorrhage.—ROUSSEAU (*Jour. méd. de Bruxelles*, 1903, No 50) reports 6 cases, the following being the most interesting:

Case I.—Three days after the beginning of menstruation the patient was seized with a severe pain in the right groin radiating down the thigh. Similar attacks followed at intervals of two months, and a tumor the size of the first developed in the cul-de-sac, which, on opening the abdomen, proved to be a large hæmatoma of the ovary.

Case II.—The patient had a sudden attack of pain, with tenderness and resistance over McBurney's point. Bilious vomiting and elevation of temperature. Several similar attacks followed during the next few months, the diagnosis of recurrent appendicitis was made, and on section a small hemorrhagic ovarian cyst was found with a twisted pedicle, the appendix being normal.

Case III.—The patient had a violent attack of abdominal pain, with vomiting and rapid increase of a pre-existing ovarian neoplasm. On section the abdomen was found to be full of blood which had escaped from a cancerous cyst. All the patients made a good recovery.

Operation for Prolapse of the Ovary.—MAUCLAIRE (*Semaine Gynécol.*, 1903, Nos. 35 and 36) describes the following operation for the relief of retroversion associated with prolapse of the ovaries which resists ordinary treatment: After opening the abdomen a slit is made in the upper part of either broad ligament midway between the uterus and the pelvic wall, the fimbria ovarica divided in order to free the prolapsed ovary, and any adhesions are separated. Any necessary conservative work is done. The ovary is drawn through this opening, which is contracted with sutures, so that the gland cannot slip back again, and, finally, the end of the tube is sutured to the anterior surface of the broad ligament near the ovary. Hysteropexy is performed to keep the uterus in an anterior position.

[Barrows, of New York, describes a similar operation, which he calls "shelfing" the ovary. Both seem to be open to the objection that the gland is not left in its normal relations and that its blood supply may be consequently interrupted.—H. C. C.]

Cancer of the Ovary in a Child.—KUSNETZKI (*Jour. Akuschi Shensk. bolesnej*; *Zentralblatt für Gynäkologie*, 1904, No. 13) reports the case of a girl, aged fourteen years, who had never menstruated. She had an

abdominal tumor of a year's standing, accompanied with severe pains. It was larger than the fist, nodular, and movable. On section it was discovered to be pedunculated and was easily removed. The patient was examined nearly two years after operation and there was no evidence of recurrence.

OPHTHALMOLOGY.

UNDER THE CHARGE OF

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PROFESSOR OF DISEASES OF THE EYE IN THE PHILADELPHIA POLYCLINIC.

Observations on Renal Retinitis.—NETTLESHIP (*Royal London Ophthalmic Hospital Reports*, October, 1903), based upon the study of quite a large number of cases of this disease, comes to the following conclusions which, however, are confirmatory of what had been previously known rather than in themselves very novel.

It is, of course, in the chronic interstitial and chronic parenchymatous forms of nephritis that albuminuric retinitis so commonly occurs. A few cases are recorded in connection with lardaceous disease and with nephritis due to inflammation of the bladder, ureter, or pelvis of the kidney; but additional cases in connection with any of these maladies are deserving of careful record. The same may be said of retinitis due to acute nephritis of previously healthy kidneys; such cases are said to occur occasionally, especially after scarlet fever.

The chief exception to this rule that the retinal changes depend upon chronic nephritis is seen in the albuminuric retinitis of pregnancy. The renal condition here is not a true acute inflammation but a rapid degeneration of the epithelium such as is found in some forms of acute blood poisoning. Kidneys so affected may rapidly pass into a state of chronic nephritis and contraction. It is very important in every case of pregnancy retinitis that the condition of the kidney before pregnancy should be known when possible. The prognosis for life in pregnancy retinitis is better than in the ordinary cases; thus, of 22 cases recorded by Nettleship only 5 are known to have died and only one of these within two years. On the other hand, of 42 non-pregnancy cases only 9 lived more than two years, and no less than 25 died within one year. The pregnancy retinitis occurs only once as a rule, and in the majority of cases after several pregnancies. There are certain cases of failure of sight *after* confinement in which the vision remains bad for several weeks and then returns more or less. The condition of the fundus during the active period is not known.

A large excess (if the pregnancy cases are omitted) are males; in the writer's series of cases the age ranged from thirty to sixty years, the most prolific decade being from fifty to fifty-nine years. In these cases,

between 80 and 90 in number, the prognosis for life seemed better when the retinitis came on after fifty-five years than before.

There are two principal factors in the production of renal retinitis, a morbid state of the blood and disease of the retinal arteries; in most cases both conditions are present. The ophthalmoscopic observer may fairly suspect an early stage of granular kidney whenever he finds decided hyaline thickening of the retinal arteries, especially in young subjects. This hyaline fibroid thickening of the retinal arteries is now well known to be indicated by intensification of the bright streak and compression of the veins where they are crossed by arteries. This condition is not always symmetrical in the two eyes nor evenly distributed in the same eye. After middle age hyaline thickening is less useful as a diagnostic sign of granular kidney. We must still take it, however, as a sign of danger of cerebral hemorrhage.

The general opinion is that the particular characters of the retinitis do not afford any guide to the kind of chronic kidney disease present. The more violent cases are chiefly toxic and the milder more chronic ones chiefly vascular in origin.

Nettleship thinks it certain that there is only one sort of renal retinitis and the many varieties of change seen during life indicates only different stages and degrees of (*a*) general œdema; (*b*) exudation into the nerve-fibre layer; (*c*) spots or patches of opacity in the deeper layers due to degeneration of fibrinous or albuminous effusion in the inner granule layers and perhaps to changes in Muller's fibres.

The optic neuritis and retinal hemorrhages so often present in varying degrees are not characteristic, though they increase the difficulty in interpreting the morbid appearances.

Other constitutional or local conditions produce retinitis resembling and sometimes indistinguishable from that caused by disease of the kidneys, of which the retinitis associated with glycosuria is particularly to be dwelt upon. In some of these cases the urine also contains albumin, and here the disease may be the ordinary albuminuric retinitis, but this is not true of others. The life prospects in the retinitis of diabetes seems better than in ordinary renal retinitis.

The typical retinitis of renal disease is nearly always symmetrical though not always equally so, and rarely the affection is confined to one eye. It is doubtful whether relapses occur, but we have proof that retinal hemorrhages are repeated in eyes that have passed through albuminuric retinitis.

Albuminuric choroiditis is mentioned by many writers. Iritis in renal disease has been seen in two cases by Knies.

Influence of Resection of the Cervical Sympathetic in Optic Nerve Atrophy, Hydrophthalmos, and Exophthalmic Goitre.—BALL (*Journal of the American Medical Association*, January 30, 1904), from personal experience and a review of reported cases by others, comes to the following conclusions: 1. Excision of the superior cervical ganglion of the sympathetic nerve is worthy of a trial in those cases of simple atrophy of the optic nerve which resist measures less heroic. 2. It is yet impossible to say whether the bilateral operation is advisable in unilateral optic nerve atrophy. 3. The value of sympathectomy in congenital hydrophthalmos has not been demonstrated. 4. In exophthalmic goitre complete excision of the cervical sympathetic is followed

by a larger percentage of cures than is any other procedure. Thus far no deaths have been recorded. The number of operations, however, is small, and final conclusions can be announced only after a large number of cases shall have been treated by this method.

A Hitherto Undescribed Membrane of the Eye and its Significance.—VERHOEFF, Boston (*The Royal London Ophthalmic Hospital Reports*, October, 1903), after a careful study of many sections arrives at the following conclusions: In the pigment layer of the retina there is a fenestrated membrane identical in structure and staining reactions with the membrana limitans externa.

The rods and cones are not nervous elements, but modified ependymal cells, and are analogous to sensory epithelium.

The limiting membrane of the rosettes of the glioma retinæ is a fenestrated membrane similar in every way to the membrana limitans externa, and the rosettes correspond to the neuroepithelium of the normal retina.

The structure of the limiting membrane of rosettes explains why they assume their spherical and spiral-like forms.

"Neuroepithelioma retinæ" is no more suitable than "glioma retinæ" for the class of tumors to which these terms have been applied.

Enucleation and its Substitutes.—GRIMSDALE (*Medical Times and Hospital Gazette*, December 19, 1903) advocates a modified form of Mules' operation. The modification consists in leaving the cornea in place and making a large curved incision above it in the sclera. The cosmetic result is excellent. There is no sinking of the artificial eye. The movements of the latter are very good, as much as one-half inch laterally and vertically almost the normal. The objections to enucleation are not only cosmetic, but the irritation caused by the prothesis is to be considered also because of the large space between it and the concave stump, in which secretion accumulates, and decomposition gives rise to chronic conjunctivitis, and finally changes in the subconjunctival tissue, so that bands are formed which render the retention of an artificial eye difficult and sometimes impossible. Attempts at improving such a stump are not likely to be successful.

The injection of paraffin into the space of Tenon is certainly not devoid of its own special risks; it has been followed in some instances by thrombosis of the neighboring veins and may thus cause blindness in the other eye.

The attempt has been made to transplant a rabbit's eye whole into the empty orbit, but it has not been successful. Even where the transferred tissues have lived, they have softened and left a very imperfect stump.

As regards the comparative safety from sympathetic ophthalmia, the advantage seems to be with enucleation; although, as is well known, many cases have followed even enucleation. Still, these, like those which have followed Mules' operation, have been of a mild type. There is no case in which sympathetic ophthalmia has followed a Mules' operation for any other condition but injury—*i. e.*, not when the operation has been performed for staphyloma or similar condition.

When enucleation is decided upon it would, perhaps, be best to use Frost's method of inserting a large glass sphere in the hollow of Tenon's capsule after enucleation and stitching it in.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

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Topographical Anatomy of the Crypts of Hypertrophied Tonsils.—Under this title DR. A. COURTADE presents an elaborate and illustrated paper (*Archives internationales de laryngologie, d'otologie et de rhinologie, Mars-Avril*, 1903) showing that the crypts, which are more numerous than they are supposed to be, exist upon the top and the bottom of the tonsil as well as in the sides and front, and that they all converge toward the interior instead of having an indefinite or irregular course. He was led to this study by finding caseous masses expressed from the tonsil beneath the anterior pillar, and so minute that they could not be penetrated by an ordinary probe.

Foreign Body in the Œsophagus Removed by Gastrotomy.—At a meeting of the Clinical Society of London (*British Medical Journal*, October 31, 1903) DR. PATTERSON exhibited an inhaler removed by gastrotomy from the œsophagus of a male phthisical patient. It measured four and one-half inches in length and almost three-quarters of an inch in diameter. Inside the metal case was a glass inhaler containing a drachm of creosote. A skiagraph showed the case lying to the left of the spinal column and almost parallel to it. It produced no symptoms whatever, as after swallowing it the patient had not taken food. When the stomach was opened, one inch of the case was projecting from the œsophagus into the stomach, whence it was removed. The patient made an uninterrupted recovery.

Removal of Nasal Polypi.—DR. ALBERT RUAULT describes and depicts (*Annales des maladies de l'oreille, du larynx, etc.*, February, 1904) his improved intranasal polypotome, in which, by pressure of the thumb, the guard is pushed down over the wire loop. This instrument would appear to be much steadier than other forms of polypotome.

Vascular Rhinopharyngeal Fibroma.—At a meeting of the Clinical Society of London (*British Medical Journal*, October 31, 1903) DR. HERBERT TILLEY showed a lad, aged sixteen years, from whose rhinopharynx he had removed a fibro-angioma by various operations. When first seen, two years before, the patient had complete nasal obstruction, with blood-stained discharge from the left nostril of five months' duration. A large, sloughy, easily bleeding mass completely filled the left nasal fossa. In November, 1901, but half the growth could be removed by Ollier's method. In December, after a preliminary laryngotomy, division of the soft palate and removal of the left side of the hard palate, all visible growth was removed, also in March, 1902,

after recurrence. In July, 1902, there was again extensive recurrence, and after preliminary laryngotomy the soft parts of the nose and face were turned upward; a large opening was made in the left canine fossa, and the lower half of the ascending process of the left superior maxilla was removed. The growth was seen to arise from the external surface of the antrum and ethmoidal region, and was completely removed. There had been no further recurrence. The boy had grown four inches, and early in the year the soft palate had been sutured.

Mucocele of the Ethmoid.—GUIZEZ reports (*Annales des maladies de l'oreille, du larynx, etc.*, February, 1904) an interesting case of ethmoidal mucocele of very large dimensions—say 3 cm. in every direction. It did not communicate with the nasal passage, and probably developed from one of the anterior cells of the prefrontal group. It was exposed by external excision and resection of the greatest part of the anterior wall, and found filled with a viscous, yellowish-brown liquid, rich in cholesterin. After curetting and careful scraping of the entire internal face of the osseous walls a solution of chloride of zinc one part to ten was applied and a drain left at the inferior angle of the wound. Recovery was prompt, without deformity, and with very little cicatrix.

Maxillary Sinusitis Due to a Dental Ectopia.—GUIZEZ reports (*Annales des maladies de l'oreille, du larynx, etc.*, February, 1904) a case in which the suppuration of the maxillary sinus was found to be due to a large molar tooth in its interior, the roots being implanted partly in the alveolus and partly in the floor of the sinus itself. This tooth was carious at the union of the neck and roots. For its liberation it was necessary to resect a portion of the alveolar process and the palatine vault. A slight buccal fistula presented for several weeks, but the purulent discharge and the subjective odor completely disappeared.

Chronic Suppuration of the Maxillary Sinus.—DR. CLAOUÉ, of Bordeaux, describes (*Annales des maladies de l'oreille, du larynx, etc.*, March, 1904) his new operation for gaining access to the sinus through the nasal passage in order to secure a thorough drainage, which he considers the chief feature of surgical treatment, more important even than careful curettage of the cavity. The operation is performed without general anæsthesia and consists of three stages, the last two of which may follow after the first immediately, or be postponed for a day or two, according to requirements.

1. The anterior two-thirds of the lower turbinated bone is removed close to the nasal wall with scissors, and the section is completed with the cold snare.

2. With a hand trephine, which is preferred to the motor, two perforations are made in the wall of the sinus about 2 cm. from the anterior extremity of the turbinate which had been removed; the intervening bridge is removed with the punch. The orifice thus made is then enlarged until it is nearly the size of the pulp end of the thumb.

3. The sinus is copiously washed out and then explored. If any diseased tissue exist sufficient to have kept up the suppuration, it is scraped with a curette with a flexible handle. A minute curettage is not

the aim of the operation. The sinus is then sponged out with chloride of zinc and tamponed for forty-eight hours with iodoform gauze.

Subsequent treatment consists in daily washing and the insufflation of non-irritant powders upon the whole interior surfaces.

The details of twelve cases are given, nine of which were cured. One remained content with this condition, and the two others were permanently relieved by opening the sinus at the canine fossa and then thoroughly curetting the interior. The place for drainage left by the first operation greatly favored this result.

Necrosis of Sphenoidal Sinus and Ethmoidal Cells.—A fatal case of necrosis of the sphenoidal and posterior ethmoidal cells, phlebitis of the cavernous sinus, pyæmia, is reported (*Journal of Laryngology, Rhinology, and Otology*, April, 1904) by DR. A. L. WHITEHEAD. The patient was a well-nourished woman, aged forty-seven years, who had enjoyed good health up to the time of the fatal illness, except for a purulent discharge from the left side of the nose, said to have followed an attack of facial erysipelas two years previously. For five weeks there had been frequent and very severe headaches and attacks of vertigo; for three days occasional attacks of vomiting, slight rigors, fever, and a general sense of malaise; for one day an uncomfortable sensation of tension in the left eye, with diplopia. There was some proptosis in this eye, and movements of the globe were restricted in all directions. In the nose, thick, creamy pus was seen descending between the septum and the middle turbinate of the left side.

Under ether the left middle turbinate was removed. The anterior wall of the sphenoidal sinus was found soft and carious, and the cavity full of pulpy material, pus, granulation tissue, and blood, the immediate posterior ethmoidal cells being similarly affected. The anterior wall of the sphenoidal sinus and the inner walls of the ethmoidal cells were removed, and the cavities were cautiously but thoroughly curetted, and then lightly packed with iodoform gauze to check hemorrhage.

Staphylococcus aureus was found in pure culture in the material removed.

The patient went from bad to worse and died of the pyæmia on the third day.

The condition was clearly one of chronic suppuration in the sphenoidal sinus and in the posterior ethmoidal cells, with an acute staphylococcic infection three or four days before she was operated upon.

Syphiloma of the Larynx.—DR. MARCEL LERMOYEZ reports (*Annales des maladies de l'oreille, du larynx, etc.*, February, 1904) a case of subglottic concentric syphiloma of the larynx just beneath the vocal bands in which tracheotomy seemed urgent. It resolved completely under semi-weekly injections of eight to twelve drops of gray oil and daily doses of more than six grams of potassium iodide.

Intralaryngeal Extirpation of Epithelioma.—PROF. ARSLAN, of the University of Padua, reports (*Annales des maladies de l'oreille, du larynx, etc.*, February, 1904) two cases in which recovery had remained permanent for four and five years respectively. He likewise details two more recent cases in which similar results have been maintained twenty months and nearly four years after operation. It will be under-

stood, as a matter of course, that these cases must have presented especially favorable conditions for such success. It likewise shows that a radical operation from the exterior is not necessary in every instance of malignant neoplasm of the interior of the larynx.

Paralysis of the Vocal Cords.—DR. L. REVOL reports (*Annales des maladies de l'oreille, du larynx, etc.*, February, 1904) a case of bilateral recurrent paralysis of the larynx due to dilatation of the aorta as verified by radioscopic examination.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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Notes on Disinfectants.—*Green Soap.* An elaborate series of experiments with various mixtures of carbolic acid and the official green soap of the German Pharmacopœia, free from free alkali and containing 44.02 per cent. of water, has been made by DR. O. HELLER (*Archiv für Hygiene*, Bd. xlvii. p. 213), who employed cultures of bacillus typhosus as test objects. His conclusions are as follows: Green soap possesses but slight disinfectant power, but it increases that of pure carbolic acid, and most markedly when the two substances are present in equal amounts. While typhoid bacilli are destroyed in twenty minutes by a 5 per cent. solution of carbolic acid, the same result is obtained by the employment of a 4 per cent. solution of equal parts of the two agents; that is, with less than half the required amount of carbolic acid alone. By analogy, one may conclude that the employment of soap in the preparation of disinfectants containing cresols insoluble in water not only brings about their solution to the required extent, but increases their bactericidal properties. This increase in power must be attributed either to the feebly disinfectant power of the soap or to the formation of a new complex compound of greater power, or the solution of the phenol (or cresol) experiences an increase in its rate of dissociation through the presence of the soap, and with it an increase in efficiency. But soap increases the bactericidal power of phenol to an extent out of all proportion to its own power in the same direction, and the mere fact of increasing solubility can have little or no influence.

Creolin. The term "creolin," says DR. SAMUEL RIDEAL (*Public Health*, December, 1903, p. 156), seems to have been invented many years ago as a fancy name for an emulsion of cresols and neutral tar oils in a soap solution, and disinfectants under this name have been sold in different parts of the world and manufactured by several firms, who have from time to time modified the nature and the proportions of the various constituents without warning to the public. Samples of creolin, purchased in Brussels, Hamburg, and London, have been tested

by him and found to have a disinfectant value varying from one and five-tenths to sixteen times that of pure carbolic acid. Chemical examination showed very wide differences in composition, which, however, furnishes no information as to their probable bactericidal value. Some specimens contain appreciable amounts of pyridine bases, which impart a very strong and characteristic odor, without contributing to the germicidal properties. He is of the opinion that if the name is to remain in the literature of the subject, a statement of the germicidal value in terms of some standard should be insisted upon in all cases.

Lysoform. Experiments with lysoform, a soft soap containing about 8 per cent. of formaldehyde and a small amount of volatile oil, conducted by GALLI-VALERIO (*Therapeutisches Monatsheft*, 1903, Bd. xvii. p. 452), bear out the findings of Symanski, Seydewitz, and others that it is slower in action than many other better-known agents. He found that a 5 per cent. solution required four hours' contact to destroy staphylococcus aureus, and that a 3 per cent. solution was ineffective against bacillus coli communis in less than forty-five minutes. SYMANSKI (*Zeitschrift für Hygiene und Infectionskrankheiten*, Bd. xxxvii. p. 393) killed staphylococci in pus with a 2 per cent. solution in five hours, and SEYDEWITZ (*Centralblatt für Bakteriologie und Parasitenkunde, I. Abth. Originale*, 1904, Bd. xxxii. p. 222) sterilized brushes infected with staphylococcus aureus and bacillus coli communis with a 5 per cent. solution in six hours, but cultures of these organisms by themselves were destroyed much more quickly. According to Symanski, lysoform is not irritant to the skin and mucous membranes, but Galli-Valerio asserts that solutions stronger than 3 per cent. cause too much irritation for local application in abdominal surgery.

Mercuric Cyanide. A series of tests of the bactericidal properties of mercuric cyanide, which is advocated in some quarters as an agent superior in some respects to corrosive sublimate, led HARRINGTON (*Boston Med. and Surg. Journal*, January 14, 1904) to conclude that this agent can hardly be classed among efficient germicides for surgical purposes. A 1 : 1000 solution was found to require more than three hours' contact to destroy staphylococcus aureus, and one of 1 : 500 exerted no bactericidal influence whatever against the same organisms at the end of a half-hour, beyond which time the experiments were not continued.

Hypochlorous Acid. Recent investigation having shown that, in solutions of chlorine containing about 0.05 per cent. of the gas, more than 90 per cent. of the chlorine exists in the form of hypochlorous and hydrochloric acids, and it appearing not improbable that chlorine exerts its disinfectant action as hypochlorous acid, DRS. F. W. ANDREWES and K. J. P. ORTON (*Centralblatt für Bakteriologie und Parasitenkunde, I. Abth. Originale*, 1904, Bd. xxxv. p. 645) undertook a research to determine the germicidal action of the acid in a pure state. Accordingly, pure preparations of the acid were made and tested, and although the results obtained were at times conflicting, owing to the instability of the preparations when exposed to light and in the presence of traces of organic matter, the germicidal activity of the acid appeared to be of the most intense character. In filtered suspension in pure water, anthrax spores were killed by a 1 : 10,000 strength of hypochlorous acid in the total mixture in thirty seconds. Watery suspensions of the spores, dried on thick silk threads, were destroyed by a 7 : 1000 solution in five

minutes, but spores of bacillus subtilis required twenty minutes. Staphylococcus aureus in suspension in pure distilled water was sterilized by a 1 : 100,000 solution in one minute, but not in fifteen seconds. A 1 : 250,000 solution just failed to kill a watery suspension of staphylococcus aureus in five minutes, but it killed a similar suspension of bacillus coli communis in between thirty and sixty seconds. In the presence of organic matter, and especially of proteids, it was anticipated that so unstable an acid would rapidly be decomposed and rendered inert; that it would prove almost devoid of inhibiting power in such a medium as bouillon; and that, up to a certain point, it would be rendered inert by the organic matter present, and, beyond it, it would kill quickly, with no extensive intermediate stage, such as is seen with phenol or corrosive sublimate, in which growth is restrained without actual death of the bacteria. Such was found to be the case, for while staphylococci in distilled water were killed immediately by 1 : 100,000, their growth in veal bouillon was restrained only by 1 : 5000, but they were destroyed within thirty minutes by 1 : 3000. Having satisfied themselves as to the intense germicidal activity of the pure acid and to the extent to which its power is impaired by the presence of organic matter, they investigated the principal methods by which it is or may be actually employed in practical disinfection, as in the form of chlorine water, bleaching-powder solutions, and mixtures of hydrochloric acid with oxidizing agents. They found that chlorine water is even more potent than is indicated by the figures of Krönig and Paul, for a watery suspension of anthrax spores, dried on quartz pebbles, was killed usually in between thirty and sixty seconds by a 0.015 per cent. solution, and in filtered suspension in distilled water by a 0.010 per cent. solution in ten seconds. The addition of hydrochloric acid to the extent of 0.4 per cent. by weight of the gas was found not to increase the germicidal power of the chlorine, but rather to weaken it. On the other hand, the germicidal power of bleaching-powder solution is increased by the addition of a weak acid (acetic and carbonic are the best) to liberate free hypochlorous acid (a strong acid liberates free chlorine). A saturated solution of bleaching-powder, containing 5 per cent. of calcium hypochlorite and so strong as to disintegrate a marine sponge in a minute, took between seven and ten minutes to destroy dried anthrax spores; but the same solution, diluted with twice its volume of 1.25 per cent. acetic acid, destroyed them in less than a minute. Hence, in employing bleaching-powder as a germicide, the addition of vinegar, or even free exposure to the carbon dioxide of the air, will be found of much value. Krönig and Paul's combination of potassium permanganate and hydrochloric acid was found to be slow (nearly four hours) in destroying anthrax spores dried on silk threads. As a substitute they tried a mixture of 1.1 c.c. hydrochloric acid, 3.7 grams ammonium persulphate [$(NH_4)_2S_2O_8$] and 95 c.c. water, in which, even after many weeks' keeping, the amount of chlorine and hypochlorous acid present amounts only to 0.008 per cent. At first the mixture is absolutely odorless, but in half an hour it has an extremely faint chlorous odor, which increases hour by hour until after three to four days it is very strong, indeed, and is that of hypochlorous acid rather than that of free chlorine. Its disinfectant value is at first very slight, but when six days old it will destroy anthrax spores in less than a minute. The mixture has the great advantage that it is colorless, transparent, and wholly devoid of staining

power. Although both mixtures act at a great disadvantage in the presence of organic matter, the persulphate mixture is considerably the more effective in the presence of moderate amounts of albuminous material. The chief use appears to lie in the disinfection of the skin, in which role it proved experimentally to be quite successful. Thus, hands well scrubbed with soap and hot water and soaked in the solution for five minutes were found to give no growths from scrapings from beneath the nails and about their roots; but it blackens and spoils metallic instruments, with which it should not be brought in contact.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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Ascending Renal Infection; with Special Reference to the Reflux of Urine from the Bladder into the Ureters as an Etiological Factor in its Causation and Maintenance.—Combining experimental investigations with careful clinical observations, Sampson (*Johns Hopkins Hosp. Bull.*, 1903, vol. xiv. p. 334) has brought out many interesting facts concerning the anatomy and physiology of the ureters and urinary bladder, and has done much to explain the origin of ascending renal infections. He finds that the vesical portion of the ureter changes under various degrees of dilatation and of intravesical tension of the bladder, and in each of these conditions there is special provision for guarding the lumen of the ureter and thus preventing a reflux of urine from the bladder into the ureter. Under all conditions of the bladder the direction of the current of urine from the kidney to the bladder is a constant factor in the prevention of ascending infection. In addition, if the bladder is distended the ureteral orifice is protected by the oblique course of the ureter, the long ureteral valve, the lateral walls of the labia of the ureteral orifice, and the mucosa of the ureter. But if the bladder is contracted the course of the ureter is not so oblique, the ureteral valve is shorter, and these factors play a less important part. On the other hand, additional protection is afforded by a puckering of the ureteral orifice, for the ureteral labia come together, and the ureteral mucosa is thrown into folds. The anatomical structure and physiological action of the ureters, as well as clinical experience, would indicate that the function of the ureters is not only to carry urine away from the kidneys to the bladder, but also to prevent fluid from passing into the ureters from the bladder, and under normal conditions it is impossible for the latter to take place. It was practically impossible,

when experimenting with dogs, to cause a reflux of urine from the bladder into the ureter with either an intact or injured ureteral orifice, or even with implanted ureters. Cases have been reported which contradict these observations, but the fact that an occasional case has been reported in which apparently a reflux has occurred, especially when nothing is known of the condition of the ureteral orifice in these instances, cannot be regarded as sufficient evidence for supposing that it may occur in all cases. In the production of pyonephrosis it is possible that organisms may be conveyed from the bladder to the kidney through the general circulation, the venous and arterial communication known as the vesico-utero-ovario-renal anastomoses, the bloodvessels of the ureter, the lymphatics, or the lumen of the ureter.

As regards blood infections, injections of culture of staphylococcus pyogenes aureus into the veins of animals demonstrated that for the development of pyonephrosis a stricture of the ureter was of great importance. It is well known that in general bacterial infections the organisms are eliminated by the kidneys, and if under such circumstances there should be a slight stricture of the ureter, infected urine would be dammed back into the kidney and produce pyonephrosis. Experimentally, this series of events does actually take place. In cystitis direct infection of the kidney through the lumen of the ureter is dependent in the vast majority of cases upon an extension of the inflammatory process from the bladder through the ureteral walls or along the lumen of the ureter. If, through inflammation or any other cause, the urine from the kidney is intercepted by a stricture or something occluding the lumen of the ureter, organisms may reach the urine which is dammed back, and rapidly travel up the ureter. Other modes of infection are possible by injury to the intravesical portion of the ureter, or possibly by a reflux of urine from the bladder into the ureter.

The reflux of urine from the bladder into the ureter may be considered an etiological factor in the causation and maintenance of renal infection only when the intravesical portion of the ureter is diseased, thus impairing its function, or when some ureteral abnormality exists.

On the Appearances and Significance of Certain Granules in the Erythrocytes of Man.—Since KÖLLIKER, in 1846, first upheld the view that in the transition of the nucleated red cell to the fully developed normal erythrocyte the nucleus gradually disappears within the cell, this subject has been widely discussed and variously interpreted. Recent observations made upon fresh unfixed blood stained by neutral red have brought out certain facts concerning peculiar granules which appear in the erythrocytes treated by this method, and which may have some bearing upon nuclear changes. Vaughan (*Jour. of Med. Research*, 1903, vol. x. p. 342), using polychrome methylene blue as a stain, has studied fresh blood from normal individuals and persons suffering from various diseases. In normal blood most of the red cells remain unstained, but a few show small granules which are colored a decided purplish red, showing a definite affinity for the chromatin staining principle of polychrome methylene blue (methylene azure). The number of these granulated cells varies under normal conditions between very narrow limits, and averages about 1 per cent. of the total number of red blood corpuscles. In cases of anæmia it was discovered that when the number of nucleated red blood cells was high, the granular erythrocytes were

proportionately increased, and in a case of pernicious anæmia during a blood crisis the granulated cells reached 18.8 per cent. The blood of newly born infants contained sometimes as much as 7 per cent. of granulated cells, but after several days they decreased to about 3 per cent. In various acute infections the granulated cells were seen in about the same proportion as in normal blood. Thus, their increase seemed always dependent upon the presence of nucleated red cells. The blood of embryo pigs contained about 17 per cent. of granulated erythrocytes. A study of the blood of geese and pigeons showed that as the nucleus of the erythrocytes degenerated, granules staining in the same manner as the chromatin of the nucleus appeared in the protoplasm and became scattered through the cell. The changes above described could not be demonstrated so readily in fixed specimens colored by Wright's, Jenner's, or Leishman's stains, and it is possible that during fixation the granules seen in the fresh preparations are broken up, and produce in the stained specimen the well-known appearance of polychromatophilia. The author after careful study does not believe that these granules are artefacts, but considers them as the remnants of the nuclear chromatin which has been set free in the red cells during the dissolution of the nucleus. Observations upon the blood platelets carried along the same lines go to show that these bodies react toward stains in precisely the same manner as do the granules in the red cells. This suggests that they too are derived primarily from the nucleus of the nucleated erythrocytes.

The Casuistry of Placental and Congenital Tuberculosis.—WARTHIN and COWIE (*Journal of Infectious Diseases*, 1904, vol. i. p. 140) discuss this important and interesting question. They report a case, together with abstracts of those cases from the literature which bear upon the subject. They show that the question of congenital tuberculosis, although definitely proved, has but 6 cases, including their own, to support it, in which the diagnosis is based upon anatomical changes and the presence of tubercle bacilli; in which the development of the lesion occurred so shortly after birth as to preclude the possibility of extrauterine infection, and in which syphilis was definitely excluded.

They also give abstracts of 35 probable or doubtful cases from the literature, which do not fulfil all the foregoing requirements, 8 undoubted and 1 probable case of placental tuberculosis, and 16 undoubted and 8 doubtful cases in which tubercle bacilli were found in the fœtus and placenta without histological changes.

In their own case the authors found miliary tuberculosis of the mother in the fifth month of pregnancy, tuberculosis of the placenta, and agglutination thrombi, containing many tubercle bacilli in the placenta and in the fœtus. As a result of their study, they conclude that the conditions of the circulation in the placental and uterine sinuses favor the collection of tubercle bacilli when present in the maternal blood, and that when the organisms are capable of multiplication, the first step in the development of tuberculosis of the placenta appears to be an agglutination and coagulation thrombosis of the maternal blood in the intervellous spaces. They believe that the syncytium possesses a certain degree of resistance against tubercle bacilli, and, although the passage of the tubercle bacilli through an apparently normal syncytium is still an open question, the senile degenerative changes in it during the later half of

pregnancy favor the passage of the organism through the syncytium. Their findings show that tubercle bacilli, virulent to guinea-pigs, may be found in the chorionic villi and fetal blood without marked pathological changes in these structures. They assume that the fetal tissues are relatively immune to the action of tubercle bacilli, and that a true latent congenital tuberculosis is, therefore, both possible and probable.

The authors believe that the commonly accepted dicta regarding congenital tuberculosis are probably extreme, and that it is not at all unlikely that it is of much more common occurrence than is generally supposed.

Islands of Gastric Mucous Membrane Having the Structure of the Glands of the Cardiac Zone and Region of the Fundus and Glands Simulating the Lower Œsophageal Cardiac Glands in the Upper Portion of the Œsophagus.—SCHRIDDE (*Virchow's Archiv*, 1904, Bd. clxxv. p. 1) has found certain gland structures in the mucous membrane of the œsophagus in 21 out of 30 cases examined. They are usually bilateral and occur in the upper portions of the œsophagus. They are difficult to find macroscopically in the fresh state, but after the œsophagus has been fixed in Müller formal solution the glands assume a deep-brown color, while the mucous membrane of the œsophagus is bright yellow. Three varieties of glands can be distinguished: one type is like the lower œsophageal cardiac glands; it appears as branched tubules situated in the mucosa and opening out by ducts upon the surface between the pavement epithelium covering the papillæ. The tubules are lined by columnar epithelium possessing nuclei placed near the basement membrane. In the ampullæ there are cells which give a definite reaction for mucus. Finally, the presence of isolated covering cells can be made out. The second type of gland resembles very closely the glands in the cardiac region of the stomach. The third type, which appears important and rather rare, practically reproduces the gastric mucous membrane, and contains glands similar to those found both in the cardiac region and in the fundus. Small lymph follicles may be found, and the entire structure seems to be identical in its histological appearance and secretory functions with the normal mucous membrane of the stomach.

The author believes that the epithelial covering of the œsophagus and of these gland structures takes its origin from two absolutely different sources. The glands are thought to develop from the entoderm, while the œsophagus is covered by ectoderm extending down from the pharynx.

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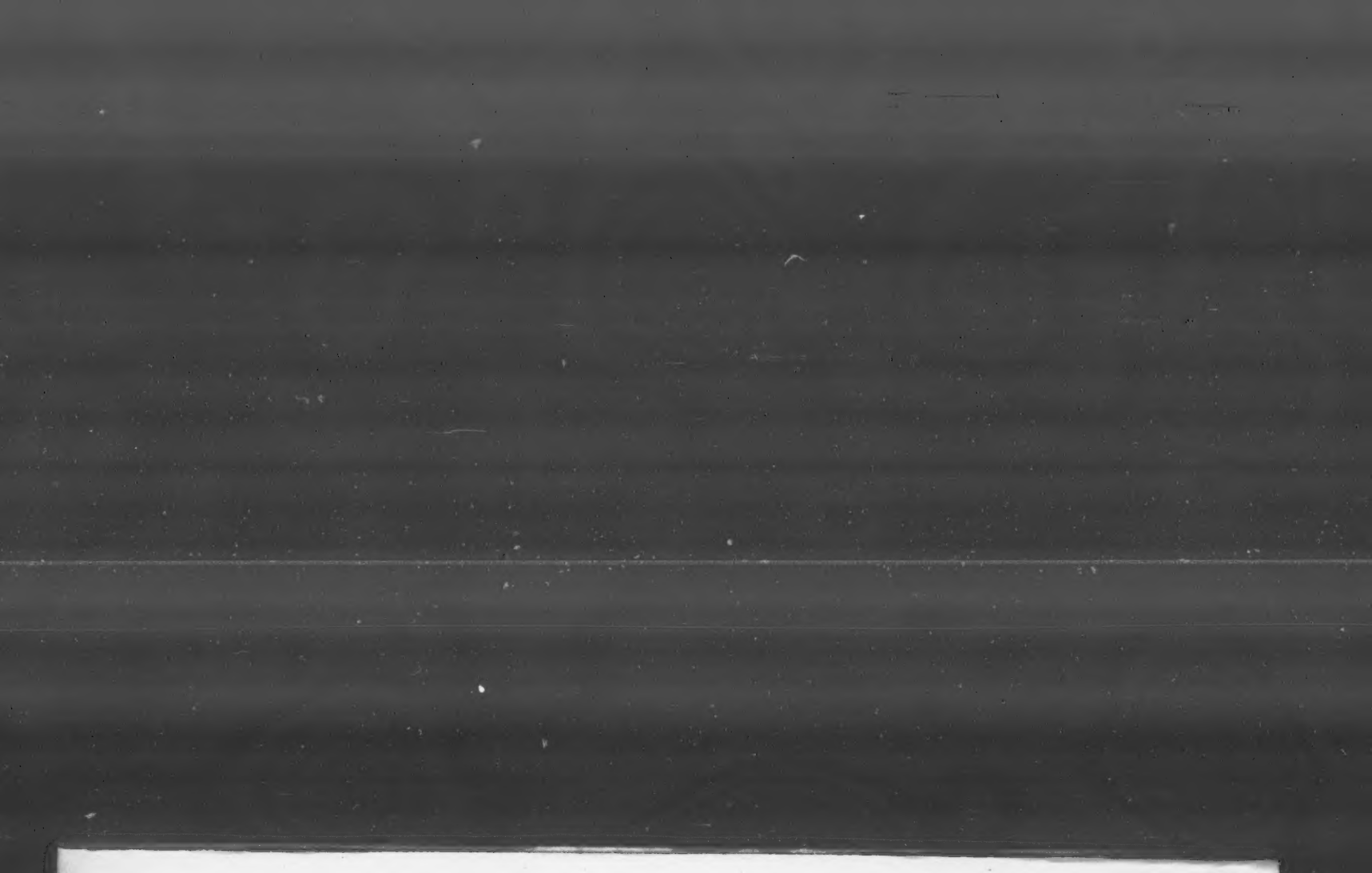

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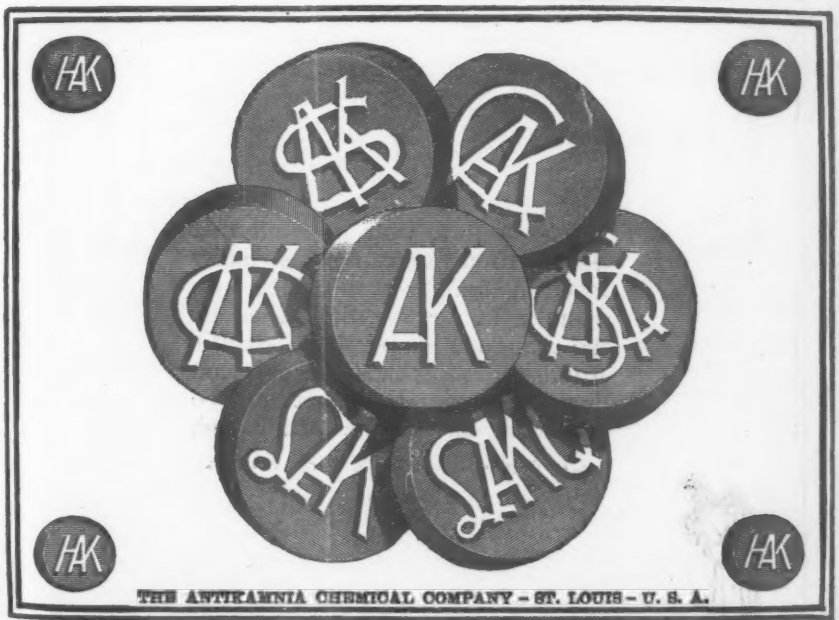

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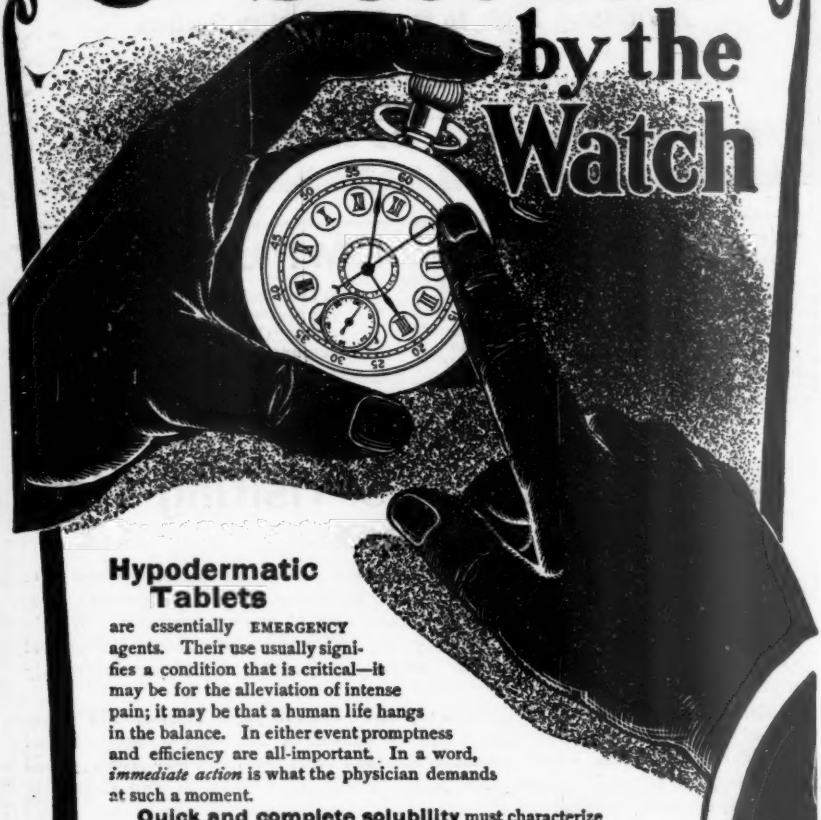

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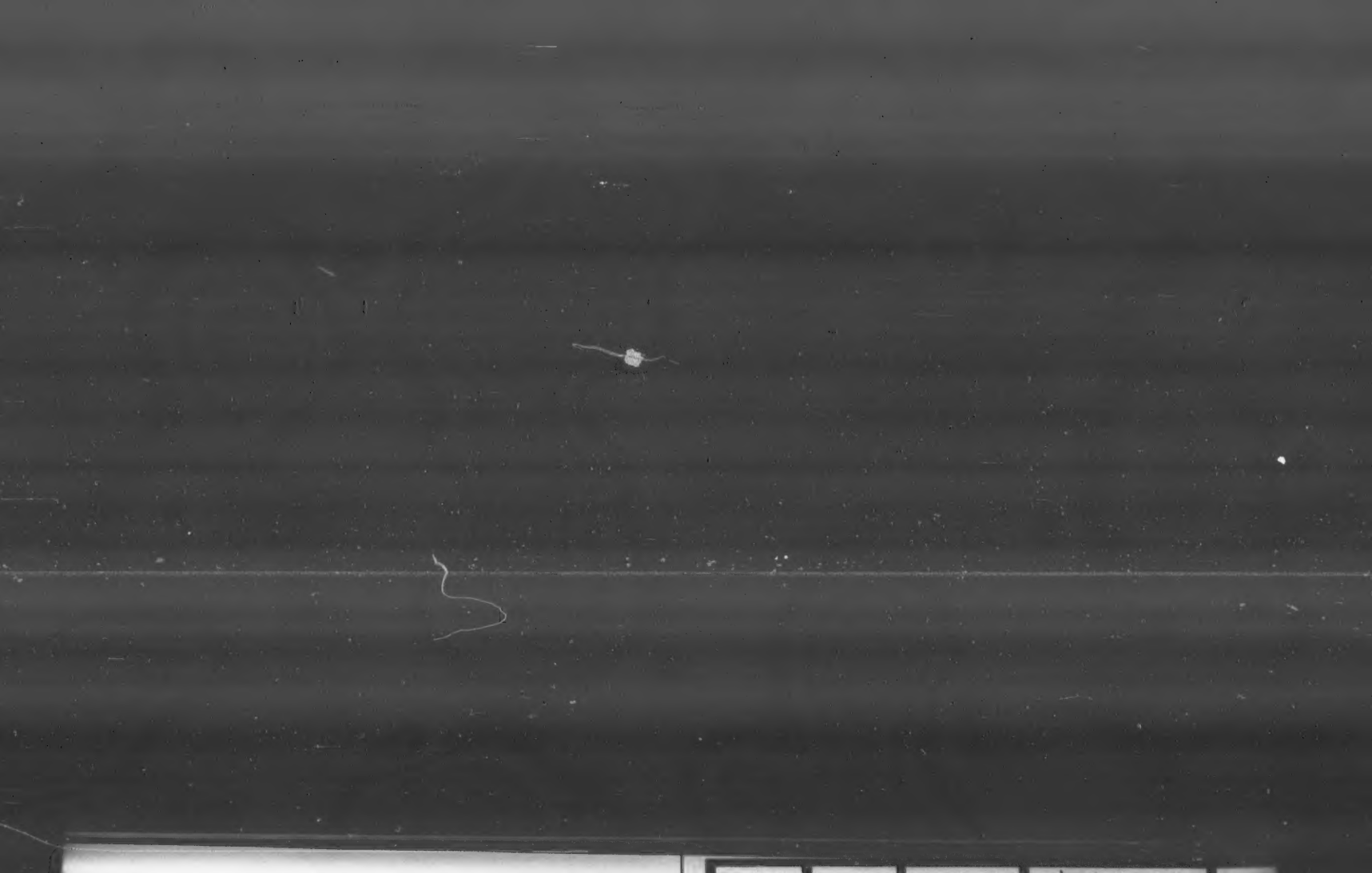

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